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## ANNUAL DISCOURSE

# *DOCENDO DISCIMUS**

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BOSTON

ONE hundred and fifty years ago this society established an Annual Lecture, known variously as the Annual Discourse, Annual Dissertation and Annual Oration. With a few exceptions, this annual communication has been presented each year, usually at the time of the annual meeting. For some reason or other the oration was omitted six times between 1813 and 1833, and again in the year 1945, when the annual meeting was canceled because of war regulations on travel. According to my calculations, therefore, 145 annual dissertations have been given, and this is the 146th, on the 175th anniversary of the founding of the Society. The subjects considered in the presentations have been diverse and have varied all the way from the practical through the theoretical and philosophical to the transcendental. In general, the chief interest of the speaker naturally determined the subject of his address, but not always. The first dissertation was given in 1804 by Dr. Isaac Rand, of Boston, "On Phthisis Pulmonalis and the Use of the Tepid Bath." A list of the names of the subsequent orators reads like a list of *Who's Who in Massachusetts Medicine*, for by custom the oration has been given each year by a member of the Society. At the annual meeting in 1835, for example, the dissertation was given by Jacob Bigelow, of Boston, the subject being "On Self-Limited Diseases." This was an epoch-making communication and was given largely in protest against the then-prevalent excessive medication. "Certain morbid processes in the human body have a definite and necessary career, from which they are not to be diverted by any known agents" is one of Bigelow's statements that should be engraved on the timeless tablets of science. The ideas expressed by Bigelow may have led to the dissertation of 1860, which caused so much discussion and dissension that the Society was induced thereafter to disclaim any responsibility for the opinions presented in the Annual Oration. This 1860 sensation was produced by Oliver Wendell Holmes's disturbing voice in a satirical but well justified protest against the almost superstitious belief that disease was a malignant agency or entity to be driven out of the body by offensive substances. One of the most quoted statements from this philippic is "It is so hard to get anything out of the dead hand of medical tradition."

It would be futile to attempt to select the most meritorious of the orations, for each has his own criteria of excellence. What one can determine, however, is the changing emphasis in the subjects of the orations as the years have progressed. Many of the dissertations in the first half century dealt with practical matters in caring for the sick, whereas in the second half century there were more papers of general interest. During both periods, however, there were ever-recurring discussions of medical education, the progress of medicine, and a few nostalgic historical papers. In the first half of the present century, there were more dissertations presented from the viewpoint of a specialist in one of the many subdivisions of medicine. Some of the more intriguing papers in the past thirty years, many of which I heard in person, were those by David Cheever in 1925, Walter Cannon in 1928, Henry Christian and Harvey Cushing in the successive years 1930 and 1931, and many others of equal virtue and more than passing interest. One "first" was recorded in 1953, when Sarah Jordan was the orator, the first woman in a hundred and fifty years to be so honored. Editor Joseph Garland gave the dissertation in 1952, substituting for John Fallon, of Worcester, whose untimely death may have been in part due to the stress and strain of preparing the Annual Oration.

The honor of being chosen an "Orator" for this society automatically calls for one's best effort. Rashly, perhaps, I decided to give up any thought of selecting my specialty as a subject for the dissertation,

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since less than 5 per cent of my potential audience would be directly concerned with radiology. Thus began the search for something new or something different that might be of interest to this audience, so widely diversified within the field of medicine. But in what other field could I speak with any authority or with any background of experience? Primarily a radiologist for almost forty years, my *alter ego* was that of a teacher for thirty-three years. And for that reason, and others that will soon be apparent, the title on the program seemed best suited. Interestingly enough, I could find no previous oration with a title in either Latin or Greek, although the leading physicians of the previous century were much more skilled in those languages than physicians of the twentieth century. But I shall not bother to translate my title for you, hoping that if you do not understand it already it shall become apparent to all as the discourse wears on.

* * *

Medical education in 1956 has many interesting facets. The three major ones are, as always: the selection and the preparation of the student; the content and arrangement of the curriculum; and the activities of the medical faculty.

One can truthfully say today that the United States has the best system of medical education the world has ever known. More time and effort are being put into the selection of the best candidates for the medical degree; they are receiving the best preliminary training they have ever had; the medical schools are larger, better equipped and more efficiently run; and the faculties are larger, better trained and more interested in producing good doctors than ever before. But there is still a large area for discussion, for criticism, for constructive suggestions, as many people join in the attempt to improve both the methods and the products of the system. Ferments are everywhere. Experiments in medical education are going on in different sections of the country and in various relations to some of the major problems. Conferences and institutes, meetings and congresses are held to define the problems, sum up the experiences and debate the recommendations that have to do with improvements in medical education.

Much of the ground has already been cultivated. The twin volumes, *Preparation for Medical Education in the Liberal Arts College,* by the subcommittee under Severinghaus, and *Medical Schools in the United States at Mid-Century,* by the Committee on Survey of Medical Education, both published in 1953, are veritable mines of fact and opinion, and give both a wider and a deeper view of the situation than could even be attempted here today. These books are outstanding mileposts along the path of improving medical education first marked out by the Flexner report of 1910. Between them, they cover the field thoroughly and in a logical manner. At the end of each chapter they state their findings and conclusions and make recommendations, but it is still quite apparent that all the problems are not yet solved and that some of the questions raised seem to have no answer as yet. The progression of affairs, both internal and external to medicine, and the passage of time, which is such an important factor in all of medicine, may eventually solve some problems but will undoubtedly raise others and new ones not yet evident.

## The Student

The selection and preparation of the student is probably the most important single factor in assuring a high-quality product, the young physician. And his selection is undoubtedly more important than his preliminary training. An excellent physician may come from a poor school in spite of limited facilities and inadequate teaching. On the other hand, a poor student may end up as a poor physician in spite of the best possible opportunities. The old adage of the silk purse from the sow's ear holds true in medical education. Admission committees vary widely on the best premedical training, and it is evident now that there is a general return to a more liberal education in college, with less concentration in basic sciences for the foundations of medical work. In other words, the hope is to educate the prospective medical student, to give him the attitudes and approach of a scholar, rather than to start him on his professional training. His *education* should, in college as well as in medical school, be concerned with study and learning for the prime purpose of understanding, not for memorizing. His *training* then would be a matter of acquiring habits, skills and technics and should properly come in his intern or resident years.

But the selection of the best of the candidates from those who offer themselves for medical school is not a simple matter of examination, interview, grades or, in fact, any predictable formula. It has to do largely with personality and character, natural ability, motivation and attitudes as well as proof of intellectual competence. All these attributes, tests for fitness and estimates of excellence are well known to the deans and the members of the admission committees, but it must be admitted that there are wide variations in emphasis in different schools and by different individuals. This is good, since it automatically prevents the turning out of a single model and favors the chance variations that may produce the exceptional physician or even the genius.

To sum up the first phase of my oration, the premedical student and his promise as a college graduate to become a good physician, I list a few of the desirable assets from the *Report of the Conference of Psychiatry and Medical Education,* held in Ithaca, New York, in 1951, published in 1952. That report states that personal characteristics and personality

traits cannot be defined accurately but that the student's principal assets are:

1) Intelligence (demonstrated intellectual capacity).
2) The ability to communicate.
3) Participation in extra-curricular activities.
4) Self-reliance.
5) Maturity.
6) Originality.
7) Curiosity.
8) Persistence toward achievement of his goals.
9) Socially acceptable aggressiveness.

I am sure that no one would disagree with these specifications, but the quantitative determination of the presence of these attributes in comparable or contrasting students may be more than difficult. The Committee wisely stated that in some areas of medicine all the traits listed above were not essential, and that the broadest possible range of selection was advisable to fit all potential situations. In the final analysis the proper selection of a future physician depends upon a careful evaluation of the balance between the qualities of human warmth (or compassion) and of pure intellectual ability. Rarely are these combined to the fullest extent in one person. When they are, selection is no problem. In the majority, however, concessions must be made in one direction or the other, the extent of which will be determined by the orientation of the selectors and the depth of the pool of selectees.

It is of the utmost importance for the future of medicine that the selection of medical students be carried out by thoughtful discussion among a group of faculty members who are sincerely devoted to the task and who represent the various views and orientations of the different medical disciplines.

There are many other problems concerned with the premedical student such as the decreasing size of the annual pool of candidates, but I must leave this subject and progress to the second phase, that of the content and arrangement of the curriculum.

## The Curriculum

The greatest source of argument and the most constantly recurring cause of faculty debate and occasional dissension is the curriculum. Dean Berry, of Harvard, points out that the word "curriculum" literally means "a running" or "a race course," and goes on to say that the present plight of the medical student reveals a new significance to the word. Since the turn of the century, or more particularly since the end of World War I, the advances in medicine and its allied fields have been phenomenal. It has been estimated that more important discoveries have been made and more valuable knowledge in medicine has been acquired in the past forty years than in all the preceding years of recorded history. And the acquisition of new facts and their use either for the protection or for the destruction of mankind continues at an ever-accelerated pace, approaching that of geometric progression. It has long since become completely impossible to teach the medical student more than a small fraction of the accumulated medical knowledge, any or all of which could be important to him in some situation or circumstance. It is obvious, therefore, that arbitrary and severe restriction and selection of material is forced upon the modern medical faculty. The difficulty comes and the arguments start when the decisions must be made how much new material must be added, what old material can safely be eliminated, and how the whole can best be rearranged. Each department head thinks, of course, that his is the most important field of all and deserves more time than has been allotted. But time is always the deciding factor, and the number of hours available eventually forces compromise. So the eternal conflict goes on. It seems to me that in general too much reliance is placed on tradition and on authority in maintaining the curriculum in its ancient patterns. But, as I have said before, the curriculum is like a football, constantly in motion, forward and back, now possessed by one group, then by the other. The ball occasionally is fumbled by a player, but it is rarely necessary to remove him. Touchdowns are scored by successful innovations either in content or in method, the rules are changed frequently, and the spectators are, in the end, the public, which decides whether it will support the teams or not. At my last belaboring of this simile the suggestion was made that *pro tempore* the psychiatrists had the ball but could not agree on the signals. They still seem to be in the same huddle.

But I present for consideration a quotation from a report of a committee of the Harvard Medical Faculty: "In modern times the constituent branches of medical science are so expanded, that they are not acquired by any physician in a life-time, and still less by a student during his pupilage." The leading word, "modern," of course, refers to the day or time when it was written, but the substance is as true today in 1956 as it was a hundred and six years ago when it was "submitted" to the members of the American Medical Association by the Medical Faculty of Harvard University and subsequently published in the *Boston Medical and Surgical Journal* of July 17, 1850! The members of the Faculty who signed the report were Jacob Bigelow (materia medica and clinical medicine), Walter Channing (midwifery and medical jurisprudence), John Ware (theory and practice of medicine), J. B. S. Jackson (pathologic anatomy), Oliver Wendell Holmes (anatomy and physiology), Henry J. Bigelow (surgery) and E. N. Horsford (chemistry). Because they seem to be quite modern in both thought and conclusion, I read a little further for possible recommendations: "Medical instruction should be adapted to the powers of the students to receive and retain what is communicated to them, and should be confined to what is important to them in their subsequent life." And

further on they say, "the length of a course of lectures is not the measure of its value to the student. It should not outlast the curiosity of its hearers."

As an epitome of their combined wisdom and experience they offer several conclusions and suggestions as follows:

> The usefulness of a medical school depends upon the education which it requires, the fidelity in exacting its own requisitions and the train of healthy exertion, active inquiry and rigid, methodical, self-regulating study to which it introduces its pupils.
>
> The subjects most important to be well taught are elementary principles . . . and the mode of thought and inquiry which leads to just reasoning . . . selecting and enforcing such practical truths as will be needed in the future . . .

Such a report would be a credit to any committee of this mid-century. The wisdom of those intellectual giants could be used in deliberations on medical education today. But what joy would those men of 1850 have if they could return today and see the tremendous progress of medicine during the intervening century!

Certainly, I could add no better suggestions than theirs for the improvement of the medical curriculum, but I should like to recommend some of the suggestions of another Orator who gave his dissertation quite recently, only fifty-two years ago. Dr. Harold Ernst, in 1904, stated that students should have the right to a community life, as claimed by all companies of scholars. He thought that a university medical school should be as compact a unit as a college of Oxford or Cambridge, and that it should afford the company of scholars the same privileges of good dormitories, good dining halls, adequate libraries and all the other facilities that then were rare and now are standard in the better schools. My emphasis here is upon the company-of-scholars idea, on the Oxford–Cambridge plan, complete with house masters and "tutors" or built-in faculty advisors, selected more for character, intellect and integrity than for technical facility or factual knowledge. Sir Lionel Whitby has come out only recently in favor of the tutorial method in clinical teaching. He advocates a "good young man" meeting his small group of students informally but regularly once or twice a week to review what they have seen, done, heard or otherwise learned on the wards or in the clinic. The emphasis would be on the integration of medicine and the basic sciences. Actually, that is already being done to some extent not only in Britain but also in the better schools of America.

To dismiss the problem of the curriculum and the host of details associated with it by the broadest possible viewpoint, I quote Rachel Carson, "our knowledge is encompassed within restricted boundaries whose windows look out upon the limitless spaces of the unknown." It does not matter so much, therefore, what one prescribes of the small part already known in the curriculum, so long as the teachers understand that it is principles, not facts, that are important. That leads me to my final section, the heart of *docendo discimus:*

## Teaching and Research

Early in this century several great changes came about in the practice of medicine, which have had profound impacts on the teaching of medicine. Chief among these were, first, the tremendous growth and development in the field of research as allied to medicine and, secondly, the change in the basic approach to diagnosis from one of observation and classification to one based on scientific "facts." The clinical change was aided immeasurably by two new medical disciplines, the medical laboratory, particularly biochemistry, and diagnostic roentgenology. The rapid development and acquisition of both knowledge and skill in these two areas, each with an ever-increasing array of tests, has promoted increasing accuracy in diagnosis. Simultaneously, the dogmatic authoritarian pedagogy declined to the point where today even the student may question the voice of authority if his scientific facts and the results of critical tests are not in order. This could also be understood as the change from the art to the science of medicine. Of course, medicine is still far from being an exact science, but it has also, in many of its aspects, become less of an art. There are even some accusations that medicine has moved more toward a trade than either art or science! Be that as it may, physicians today are certainly able to depend less on intuition and more upon scientific facts than ever before in medical history.

But this change raises the immediate problem of how much of these new disciplines should be taught to the medical student. The best answer probably is that only the application of the results is important to him in general, unless he wants to enter one of those fields. This would best be done in his postgraduate years. It is important for the student to know how such testing methods are performed, the principles on which they are based and the measure of accuracy in their applications, rather than to learn how to do them all himself, which would be practically impossible. Some tests or examinations are so conclusive in their results that they might be classed as pathognomonic or indubitable, and these are increasing in number. But as long as human beings retain the "infinite capacity for variation" characteristic of biologic material one cannot claim medicine to be an exact science. As teachers, therefore, physicians are forced to select and choose what they deem to be important for communication to their students. The good teacher is thus forced to concentrate his material and to select those portions exemplifying methods of analysis on the one hand, or principles of human biologic responses on the other. He must attempt to educate his students in principles

and in modes of thinking rather than in memorizing facts, details of cases or methods of instrumentation. Thus, clinical teaching must be integrated with the basic sciences in which systematized knowledge is the teacher's goal. Medical education should, after all, be more education than medicine, as Flexner says. In the face of the overwhelming mass of material available to be taught, better teachers are needed, to teach less. The good teacher in any field is a skilled craftsman in the art of teaching. He knows how to impart his own insight to others, to fire them with his enthusiasm and, best of all, how to help his students learn how to do their own thinking.

In one of the symposia on teaching, the attributes of an able teacher were defined thus: first, he must believe in his subject with passion and curiosity; secondly, he must love young people and want to share his knowledge and his researches with them; and, thirdly, he must respect his craft as a teacher and constantly strive to improve himself in knowledge and art. One of my predecessors wrote, "teachers need to study and to learn to avoid stagnation. No cow can be milked indefinitely without being put to pasture." (The writer must have been a city physician, for any country boy knows that it takes more than fresh pasture to keep the milk flowing!) An editorial on part-time teachers expresses it clearly: "Both the faculty and students are in fact students working at different levels of education."

As to the spirit and mechanics of teaching there are almost as many methods and ideas as there are articles on the subject. Anatole France has epitomized teaching with "The whole art of teaching is only the art of awaking the natural curiosity of young minds for the purpose of satisfying it afterwards." Harvey Cushing, however, in his *Clinical Teacher and the Medical Curriculum*, says: "It is the business of the teacher to *arouse* curiosity not to satisfy it." A similar concept is the advice for the teacher to "open the door of knowledge for the student, turn on the light, but let him see for himself the beauties therein." The capacity for absorbing knowledge, however, varies a great deal. Increased capacity for absorption may be inherited, but it can also be increased by rigorous mental discipline. By far the larger part of knowledge must be imparted or transmitted by the slow, painful process of study. Perception varies, as does imagination, both essential to teacher and student. In my own field of diagnostic radiology I have often insisted that a good imagination is a decided asset in many ways, but the corollary is that the imagination must be under cerebral control lest it run away with the facts and wreck the conclusions. After all, imagination may be only the capacity to rearrange facts, as Bill Bean says, to show a new truth, or, as I would add, to open up a new theory.

Skepticism in both teacher and student is also a decided asset if present and used in a healthy manner. Anatole France called it "The faculty of doubting," claiming it was rare among men. He wrote, "A few choice spirits carry the germs of it in them, but these do not develop without training." Henry Christian urged the application of "healthy scepticism" in all work but particularly in reading and in teaching. He said, however, in caution against its misuse, "to doubt is desirable; not to try would be reprehensible."

In my own experience of using the tools of diagnostic roentgenology as viewpoints in teaching medicine, I have employed technics gradually acquired from many sources and constantly modified to meet changing situations. One of the most effective methods of teaching is in small groups with each member of the group participating. It helps awaken interest and curiosity to challenge the student's attention in front of a roentgenogram by asking him as a representative of his group, "How old was this patient?" "What operation has he had?" "What is his probable racial background?" All are simple questions with the answers plainly evident on the film. Roentgenology is a natural-born teaching tool through which many things are visible. One attempts to inculcate the idea that observation reveals morphologic changes that can lead to thinking in terms of pathologic physiology, followed by etiologic deductions and, finally, if the student is advanced enough, an estimate of what can be done about the problem that the patient presents. One usually deals only with the shadow of the patient rather than the substance, but I am continually amazed at how much one can discover and how accurately one can foretell morphologic, functional or etiologic abnormalities. Visual methods of teaching surpass those of any other medium. That is one reason why the roentgenogram can be so useful in teaching. Students should be warned that they can believe less than half of what they hear, and not more than half of what they read, but can trust most of what they themselves see, unless it be pictorial advertising or television. After all, seeing is believing, and one picture is worth a hundred words — two are worth a thousand.

For larger audiences or classes in clinical exercises another gambit for good teaching is the planned argument between staff members over basic principles or on popular beliefs. This we have employed for years in our clinics and conferences to the benefit of successive generations of students. Dr. Wolbach and I often fought bitterly in public, mostly between ourselves at clinicopathological conferences or x-ray conferences, but sometimes we combined forces and attacked some foible or some weakness in the armor of physician or surgeon. The students were delighted and often carried on the investigation of the questions we had raised, to their own benefit. In public we were bitter enemies, in private the best of friends and companions. One discerning physician from Iowa characterized our conference arguments by stating, "You men fight like brothers."

Exaggeration for emphasis plays a good role in teaching, and honest or benign dogmatism must be used at times when it is justified. After all, 90 per cent of medical students want and need a solid foundation of accepted beliefs, basic principles and approved methods lest they be discouraged by the much vaster area of the unknown. Only the exceptional 10 per cent can thrive and be stimulated by having the large gaps in knowledge emphasized and possible avenues of approach to more and better information suggested.

As an illustration of the use of exaggeration for emphasis I cite the visual parable I have used for years in starting my lecture to the students on pulmonary tuberculosis. Telling them at the outset that it was most important to diagnose tuberculosis in the early curable stage, and that they should know the truth about the only way the diagnosis could be made, I would show them a lantern slide of a large, imposing building and ask for guesses about what it was. It was the church of Ste. Anne de Beaupré in Canada. Next I would show them the shrine in the church with innumerable crutches, which had been left as tokens of many cures that had been effected there. By this time the class would be thoroughly puzzled but wide awake and interested, waiting for the denouement. Next came a slide of an x-ray machine or a fluoroscope and then one of numerous stethoscopes hanging on the walls of the x-ray room. A simple statement that "Those are the votive offerings of many physicians who thought they could diagnose tuberculosis in its early stages without x-ray help" would point the moral that few would forget. It was really a prolonged battle, starting with World War I, to get that fact established, but now it is accepted everywhere as obvious truth.

Two principles of teaching, the importance of which cannot be emphasized too strongly, are the clarity and simplicity of presentation and the enthusiasm with which it is presented. After all, enthusiasm is the vehicle that carries the material to the student. One can often present the clinical (and sometimes even the basic) material to the student as a problem to be solved, and adopt the methods of a Sherlock Holmes in unearthing and recognizing clues, some of which may be but "acid-fast herrings" while others may lead eventually to the culprit. An example of this approach in teaching is the strange case of "Who Killed the Pheasant?" This was first used at a meeting of the College of Physicians here in Boston about thirty years ago. I told the story, with picture and diagram on slides, how three of us all shot at a cock pheasant but no one could be sure who had downed him, for five shots were fired but only three reports were heard. Obviously, there had been two simultaneous shots. Ordinary hunters would have settled the question by tossing or matching coins, but in our case I found that each hunter was using different-size shot, one number 8, another number 6 and I was using size 5. It was a simple matter to take the bird to the hospital, take an x-ray film and find that only size-5 shot were in his vital parts!

The moral was that "We see only what we look for, but we look for only what we know."

The "retrospectoscope," a theoretical instrument invented in Boston, is of great value on occasions when one goes back over a case using hindsight as an aid to diagnosis. Furthermore, the importance or significance of things to the patient must always be kept in mind and must always be emphasized to the students. Never will I forget a lesson I learned from Professor Wenckebach when he visited the Brigham more than thirty years ago. I was young in my specialty but proud of its accomplishments and jealous of its potentialities. Having found a striking calcareous pericarditis in a young woman in whom no abnormal physical signs were demonstrable, I asked to have him go over the patient and see if he could make the diagnosis. The great man was told the problem. To my surprise and discomfiture he did not percuss or auscultate the heart, but simply said, "If she has a constrictive pericarditis and *if it is causing her any trouble,* she will have an enlarged liver." He then proceeded to feel for and percuss the liver. It was not enlarged. He concluded, "The patient may have calcareous pericarditis but if she does it is not doing her any harm. Let us proceed to the next patient." I slunk away defeated but wiser thereby.

## Research

A large volume could be written about the part played by research in modern medical education. There is no doubt that the acquisition or discovery of new facts is one of the most important duties and privileges of all faculty members, and, whenever possible, the intellectual stimulus of research should be inoculated into medical students. The main objectives of the physician are and always have been the prolongation of life; the relief of suffering; the prevention and control of disease; and the promotion of the health and well-being of man. The dilemma noted by Jacob Bigelow in 1835 — "in many cases disease is more easily understood than cured" — still obtains. Since that time medical science has prevented some diseases, controlled others and cured many, but the majority are still beyond the four objectives of the physician. Research holds out the promise of eventual attainment of these goals. But my major concern is how research affects teaching, and not to record its amazing development and its phenomenal growth in my own period of time. Its present status carries dangers and threats as well as promise. Budgets are inflated, balances are upset, and judgments are influenced by pressure for publication of research work. The choice of men for appointment or for promotion on the medical faculty is often influenced by the number or size of the candi-

date's publications. Their value is seemingly estimated by the pound rather than by worth of content. Research institutions are springing up all over the country, and large foundations are sponsoring and subsidizing investigation. The direction of the search, however, is often determined by the grantor. The federal government is the largest of all donors for research covering the widest variety of projects. This may be good, but is not wholly so if it deleteriously affects medical teaching. Many men who are excellent investigators make very poor teachers. On the other hand some good clinicians who have rarely if ever written a paper may be excellent teachers. Hospitals have taken the bait of easy money, and some now have more men and money working on research projects than they have for care of the patients and teaching. The medical schools, by contrast, are losing men to foundations or other institutions, even to commercial organizations where salaries and other inducements can be made more attractive. By contrast with the sacred or hallowed aura surrounding the "pure" research man, too little attention is paid and too little value attached to skill in the art of pedagogy. But there are other compensations for the teacher, particularly the clinical teacher, of whom I sing.

### The Part-Time Clinical Teacher

Most of the burden of clinical teaching is borne today by the part-time clinical teachers. They outnumber the full-time members of the faculty but are rarely accorded the honor or the support given to the full-time men. They get little if any salary from the medical school but are supported almost entirely by either the hospital (hospital full-time group) or the hospital and their own private practice. Many get no salary, or only a "stipend" from either medical school or hospital, and yet contribute significantly to the total sum of educational endeavor. These part-time men may also add considerably to the prestige of their medical school and hospital by clinical investigation or the publication of articles or books in their chosen fields, but most of all they contribute in the testing or application of the many discoveries and the new knowledge contributed by the research group. There is now available a considerable amount of valuable information which has never been used in the care of the sick patient. The application of the discoveries is the prime function of the clinical man who is both teacher and investigator. As Cushing said in the Annual Oration for 1931, "No idea is wholly new; what *is* new is getting people to adopt it and act upon it." And in the same article he continues, "In science, credit goes to the man who convinces his contemporaries, not to him who first propounds the idea." Unfortunately, however, few of the clinical teachers ever receive their just awards for being good teachers, either from their university, their faculty or their fellow teachers. They do not want or need salaries or increased income, since most of them make enough from practice. They receive admiration, gratitude and sometimes devotion from pupils and disciples, and on rare occasions have an institution, a professorial chair or an endowed fund named for them. For the great majority of part-time clinical teachers, however, a little more regard by faculty and colleagues, some moral and financial support for their work and some official recognition would be the logical and proper reward for an important job well done. My colleague, Sam Levine, is an excellent example of the good part-time clinical teacher. For forty years he has made careful observations on patients, written down his findings and his conclusions and then later recorded the results of his treatment. He has investigated many problems, written many articles and several books and has made many contributions to the knowledge of heart disease. He has applied many other discoveries to his own problems. But his greatest contribution has been his enthusiastic teaching of medical students, of house officers and residents, and of colleagues, fellow staff members and many graduate physicians who seek instruction from him year after year. Medical students have come under his influence only two out of their four years, and house officers two to five years; but his postgraduate teaching has gone on for forty years. Largely owing to the efforts of men like Paul White and Sam Levine the understanding and treatment of heart disease are better than in any other special field of medicine, with almost equal knowledge and competence spread widely over the entire country.

The part-time clinical teacher has many other activities of value to medical education as well as to medicine in general. He may act as the spokesman for medicine in politics and in law; he may secure large sums for medical education or research through his contacts with influential persons or from appreciative patients; he may persuade the exceptional young man to enter medicine; and he may make the greatest contribution of all to medical education simply by the power of splendid example, for there is probably "nothing in the teaching of medicine as important as example."

Every physician should be an investigator, for, by reason of its nature, much of medicine becomes an experiment. By watching and studying the progress of disease or its alleviation or cure, he naturally acquires knowledge. There is no greater satisfaction to the teacher than the acquisition of knowledge. There is a high index of intellectual gratification and spiritual contentment in both teaching and learning. The intellectual capacity and originality of the men and women who make up the faculty and the student body of the modern medical school are almost guarantees of suitable recompense at the intellectual level. The atmosphere of a university medical school pro-

vides endless opportunities for the faculty to teach each other and to enlarge each his own store of knowledge as well as to broaden his outlook.

The full employment of one's faculties somehow brings contentment and happiness. Added to this is the joy of learning, and the pleasure of watching the growth of the "intellectual progeny" partly under one's care. This is an immeasurable pleasure similar to that of the orchardist who plants his carefully selected stock, nurtures it with measured and proper sustenance, and watches it grow and develop and eventually bear fruit. To me it seems that the medical teacher lives a highly satisfactory existence, obtaining recompense in spiritual values if not in worldly goods, and contributing largely to the success of the institutions to which his time and effort are devoted. Not the least of these compensations are the warmth of affection of his disciples and his own reciprocatory pride in their progress and accomplishments. Some of them accept similar responsibilities in university medical schools and carry on the principles, precepts and pleasures turned over to them. Not the least of these compensations is *docendo discimus*, "we learn by teaching."

I close with the best description I could find of the product that all are striving to create or produce: the educated man. This is the definition given by Woodrow Wilson, the humanist and educator, who wrote: "The end objective of education, even at the postgraduate level, is not so much technical proficiency as character. Moral integrity is still our most important product."

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# TREATMENT OF CHOICE IN CANCER OF THE UTERINE CORPUS*

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CANCER of the uterine corpus can be successfully treated in a number of ways. However, there is no unanimity concerning the best therapy. The following discussion is intended to evaluate the different methods and to aid in the development of a plan for the treatment of this disease.

The types of treatment now employed are: total hysterectomy by either the abdominal or the vaginal route; radiotherapy; a combination of these two; and radical hysterectomy. These can be evaluated by their applicability, primary mortality and five-year survival without evidence of disease. Because the various methods of treatment are not equally applicable, the resulting selection tends to influence the primary mortality and cure rate. For this reason, it is desirable to arrange similar cases into clinical classifications that will allow less distorted comparison.

There are a number of systems of dividing cases into comparable groups. The International Classification is used here. Stage 1 comprises patients in whom, on clinical evaluation, the growth is confined to the uterus; Stage 1, Group 1, consists of cases that are clinically operable; in Stage 1, Group 2, the lesions are technically operable, but the patients are in poor general condition (that is, bad operative risks); and Stage 2 includes patients in whom the growth has spread outside the uterus — that is, the lesion is inoperable.‡

In the *Tenth Annual Report on the Results of Treatment in Carcinoma of the Uterus*, data from 27 clinics on 8366 cases are recorded.[1] Fifty-three per cent were Stage 1, Group 1, 33 per cent Stage 1, Group 2, and 14 per cent Stage 2. The over-all five-year cure rate was 54 per cent; the rate in Stage 1, Group 1, was 69 per cent, that in Stage 1, Group 2, 46 per cent and that in Stage 2, 20 per cent.

## PRIMARY HYSTERECTOMY

Surgical excision is the oldest and most direct method of treatment. Any more limited procedure than total hysterectomy is to be condemned as inadequate. Abdominal hysterectomy is to be preferred, because the tubes and ovaries can be easily removed at the same time, the uterus taken out with a minimum of pressure and manipulation, and the peritoneal cavity freely explored to enable one to recognize metastases.

The tubes and ovaries are the seat of metastasis in some 5 to 15 per cent of cases.[2,3] Therefore, if the uterus is to be removed, the adnexa should also. Squeezing or undue motion of the uterus during hysterectomy probably increases the likelihood of dissemination. For, if the tumor lies in the lymphatics or venous spaces, intermittent compression could dislodge and propel bits of tumor beyond the field of ex-

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‡Excluded from consideration here are the adenocarcinomas that involve both the corpus and the cervix. Those cases are designated carcinoma corporis et endocervicis, and they are segregated in accordance with the policy of the annual report on the results of treatment in carcinoma of the uterus.[1] These cases have a poorer prognosis than carcinoma of the corpus and *should be treated as cancer of the cervix.*

cision before the pathways are interrupted. The recognition of hepatic or other metastasis is rather academic as a rule, but occasionally the removal of isolated metastasis is possible and worth while, and the information may be of some value in election and direction of x-ray therapy. For all these reasons, vaginal hysterectomy is a second choice to the abdominal approach. The tubes and ovaries can be removed by the vaginal route, but the procedure is somewhat hazardous because of their distant attachment and the ever-present risk of escape of the vascular pedicle before it is securely ligated. Bastiaanse[3] failed to remove one or both ovaries in 33 of 114 cases treated by vaginal hysterectomy — that is, 29 per cent. Because of the confined avenue of approach, the manipulation of the uterus is inevitably more than is required during laparotomy, and, of course, only the pelvic peritoneum can be adequately explored through the vagina.

TABLE 1. *Frequency of Hysterectomy for Carcinoma of the Uterine Corpus.*

| SOURCE OF DATA | YEARS WHEN TREATMENT PERFORMED | DATE OF REPORT | TOTAL NO. OF PATIENTS SEEN | NO. OF PATIENTS OPERATED ON | REMARKS |
|---|---|---|---|---|---|
| McKelvey & Tompkins[4] | 1947-54 | 1955 | 142 | 124(87.5%) | With and without radiation |
| | 1939-46 | 1955 | 156 | 110(71%) | With and without radiation |
| Taylor & Becker[5] | 1926-40 | 1947 | 336 | 134(40%) | With and without radiation |
| Kimbrough[6] | 1937-50 | 1954 | 115 | 66(57%) | With and without radiation |
| Waterman et al.[7] | 1936-45 | 1952 | 126 | 95(75%) | With and without radiation |
| Cosbie et al.[8] | 1937-47 | 1954 | 175 | 68(39%) | With and without radiation |
| Bastiaanse[3] | 1938-52 | 1952 | 264 | 250(95%) | 217 vaginal; 33 abdominal. |
| Kimbell[9] | 1938-53 | 1954 | 245 | 221(90%) | |
| Winterton[10] | 1940-54 | 1954 | | 90(95%) | Wertheim-type operation |
| Rickford[11] | 1943-48 | 1954 | 147 | 120(81.6%) | |
| | 1949-53 | 1954 | 174 | 152(87.4%) | |
| Hawksworth[12] | 1942-54 | 1954 | 184 | 164(89%) | |
| Present series | 1927-50 | 1956 | 518 | 360(69%) | |

The great advantage of the vaginal hysterectomy lies in its applicability to the very obese, poor-risk patient. In such cases the procedure carries a lower morbidity and mortality than the abdominal approach.

The frequency with which hysterectomy is used is determined not only by the extent of the disease and the general condition of the patient but also by the enthusiasm of the operator. Many conditions are only relative contraindications. Diabetes, hypertension, obesity, and advanced age are factors that, in their most exaggerated state, absolutely preclude hysterectomy, but in lesser degree may be regarded as contraindications in one clinic and not in another. A number of clinics have succeeded in pushing their operability rate to around 90 per cent (Table 1). That this is possible, even in the relatively poor material of a state hospital, is attested to by McKelvey and Tompkins.[4] In this clinic, 69 per cent (360 of 518) of the patients were operated upon in the years 1927 to 1950.

Hysterectomy, either alone or in conjunction with preliminary radiation, carried a remarkably low mortality. In the collected series of 853 cases, there were 24 (2.8 per cent) operative deaths (Table 2).

In the tenth annual report, a comparison of the results in institutions favoring hysterectomy and those largely employing radiotherapy shows a 57 per cent and a 53 per cent five-year cure rate respectively,[1] in a sample of about 3000 cases. These over-all results do not, however, give precise information concerning the efficacy of hysterectomy itself. Table 3 lists the results from 10 clinics where the different forms of treatment are applied, showing that primary hysterectomy alone produced a 67 per cent cure rate, with no appreciable difference between clinics where it was used exclusively and those where it was selectively applied. McKelvey and Tompkins[4] have indicated that the cure rate will rise as the proportion of cases treated by total hysterectomy is increased. Accordingly, they conclude that strenuous efforts should be made to increase the frequency of operation. Vaginal hysterectomy as represented by Bastiaanse's[3] series of 83 cured in 115, or 72 per cent, is comparable to the results of abdominal hysterectomy.

## RADIOTHERAPY ALONE

Radiotherapy for carcinoma of the corpus has never enjoyed the same measure of popularity that it has in cervical cancer, largely because surgical treatment of cancer of the corpus is fairly effective. This lesion was first treated with a single cylindrical radium applicator placed in the uterine canal. Because the endometrial cavity was frequently large and at times irregular, several containers of radium were inserted in the hope of covering the tumor-bearing surfaces more thoroughly. This evolution was carried one step farther by Heyman and his associates,[22] who devised a series of relatively small ovoid radium containers that could be used to fill the uterine cavity completely. The radium could be placed in various-sized jackets to make the dosage more comparable — that is, if the cavity was large, a large-sized jacket was placed about each radium source, and if it was small, a smaller jacket was used, so that in each case about the same number of radium sources was packed in the uterine cavity. From experience, Heyman et al.[22] had found that about 1500 milligram hours, in an average-sized uterus with the use of 10 applicators with medium-sized jackets, given on two successive

occasions three weeks apart, was an effective dose. To develop a comparable dosage scheme for uteri of other sizes, he postulated that the critical area is the peritoneal surface of the uterus. There, one should give about the same dose in each case. The uterine wall was regarded as 2 cm. thick, and by measurement of the arrangement mentioned above, — that is, 10 applicators with medium-sized jackets for 1500 milligram hours, — it was found that the dosage at 2 cm. was 1500 gamma r. Then, by means of various-sized cavities and various-sized radium containers, a table was worked out that would allow the easy calculation of an equivalent dose for any number of applicators of any size. In recent years the dose has been increased somewhat. After the uterus is packed at one of the sessions, a large cylinder containing radium is inserted in the vagina. It delivers a small dose of about 1000 milligram hours, to deal with possible vaginal recurrence.

The advantage of the radium treatment is that it can be applied to patients whose general condition or extent of local disease precludes operation. It is a less strenuous procedure that can be done with a minimum of anesthesia. In view of the frequency of obesity, diabetes and advanced years in this disease, the radium treatment is not to be ignored. A minor disadvantage is that multiple uniform sources in graded sizes are not widely available. To realize the maximum efficiency with radium, that apparatus is required.

When radiotherapy is used, the patient must be followed closely, and if any sign of recurrence (such as pyometrium, bleeding or palpable tumor) is noted, prompt hysterectomy should be performed if at all possible. Patients in whom operation is done in this situation have a remarkably good prognosis, as witness a five-year cure rate of 62 per cent in 90 cases at the Radiumhemmet.[18]

The advanced case with clinical invasion of the pelvis, or distant metastases that make hysterectomy inadvisable, is a poor candidate for any treatment, including radiotherapy. However, radium and x-rays are the treatment of choice and more effective than one might expect, as judged by a 20 per cent five-year salvage in 1135 treated Stage 2 cases recorded in the *Tenth Annual Report on the Results of Treatment in Carcinoma of the Uterus.*[1]

Radiotherapy is generally conceded to carry the least risk, and indeed this is borne out by the finding of only 14 deaths in a combined series of 969 cases — that is, 1.4 per cent (Table 2). This low mortality is an index of the risk of the method, for radiotherapy is employed no matter how serious the disease or how poor the patient's general condition. Actually, of course, there are occasional patients too ill even for radiotherapy — for example, in the Radiumhemmet series of 708 patients, 13 (1.8 per cent) were given no treatment.

The results of radiotherapy alone in clinics where the various treatments are selectively employed

TABLE 2. *Primary Mortality with Treatment of Carcinoma of the Uterine Corpus.*

| SOURCE OF DATA | YEARS WHEN TREATMENT PERFORMED | DATE OF REPORT | MORTALITY WITH RADIATION ALONE* | MORTALITY WITH RADIATION FOLLOWED BY HYSTERECTOMY* | MORTALITY WITH HYSTERECTOMY* | WERTHEIM PROCEDURE | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | OPERATIVE MORTALITY* | INCIDENCE OF FISTULA* | INCIDENCE OF NODES AFFECTED* |
| Corscaden & Tovell[12] | 1938-48 | 1954 | 1/57 | 2/217 | 0/62 | | | |
| Tailhefer[14] | | 1952 | | | 4/101 | | | |
| Brunschwig & Murphy[15] | 1947-54 | 1954 | | | | 0/57 | 6/57 | |
| Way[16] | 1931-38 | 1951 | | | 2/42 | | | |
| Hurdon[17] | 1925-37 | 1942 | 1/156 | | | | | |
| Kimbell[9] | 1938-53 | 1954 | | | 6/221(2.7%) | | | |
| Winterton[10] | 1940-54 | 1954 | | | | 3/90 | 0/90 | 2/28 |
| Rickford[11] | 1943-48 | 1954 | | | | 2/17 | | 4/17 |
| Hawksworth[13] | 1942-54 | 1954 | | | 8/164(4.9%) | | | |
| Bastiaanse[3] | 1938-52 | 1952 | | | 2/217 (vaginal)† 2/33 (abdominal)† | | | |
| Kottmeier[18] | 1936-45 | 1953 | 8/695(1.3%) | | | | | |
| Kimbrough[8] | 1937-50 | 1954 | 4/47 | 0/60 | 0/8 | | | |
| Scheffey et al.[19] | 1940-45 | 1946 | 0/14 | 0/26 | 0/5 | | | |
| Totals | | | 14/969(1.4%) | 2/303(1%) | 24/853(2.8%) | 5/164(3.0%) | | |

*Expressed as no. of deaths per no. of cases treated.
†Up to 70 days postoperatively.

(Table 3) are inferior to those in the surgical groups, partly because of selection, which relegates the worst cases to radiation. The 62 per cent cure rate at the Radiumhemmet is not quite so good as the 65 per cent salvage in the exclusively surgical clinics, presumably owing to preselection of material — that is, patients with more favorable cases tend to be sent to the surgical unit. However, it compares favorably with the 55 per cent cure rate that is the combined little influence on the vaginal growths that subsequently developed. It is generally conceded[16,23] that such growths arrive there by veins or lymphatics and not by surface implant, but nevertheless might have been disseminated at the time of operation. In an effort to cope with this problem, preoperative radiation was introduced and became popular in the thirties. As a rule, radium (1500-6000 milligram hours) was applied, and six weeks later the hysterectomy was

TABLE 3. *Cure Rate* in Carcinoma of the Uterine Corpus.*

| SOURCE OF DATA | INTERVAL OF TREATMENT | YEAR OF REPORT | CURES AMONG ALL PATIENTS SEEN | CURES AMONG PATIENTS TREATED WITH RADIUM & X-RAYS | CURES AMONG PATIENTS TREATED WITH RADIUM ALONE | CURES AMONG PATIENTS TREATED WITH X-RAYS ALONE | CURES AMONG PATIENTS TREATED WITH RADIATION FOLLOWED BY HYSTERECTOMY | CURES AMONG PATIENTS TREATED WITH HYSTERECTOMY | CURES AMONG PATIENTS TREATED WITH RADICAL HYSTERECTOMY | CURES AMONG PATIENTS GIVEN OTHER TREATMENT |
|---|---|---|---|---|---|---|---|---|---|---|
| Winterton[10] | 1940-48 | 1954 | 45/61 | | | | | | 45/57 | |
| Bastiaanse[2] | 1938-47 | 1952 | | | | | | 83/115(72%), vaginal; 14/24, abdominal. | | |
| Hawksworth[12] | 1942-49 | 1954 | 59/98 104/159(65%) | | | | | 56/87 153/226(68%) | | |
| Rickford[11] | 1943-48 | 1954 | 92/147 | | 3/18 | | 4/4 | 76/103 | | 9/22 |
| Kimbrough[6] | 1937-46 | 1954 | 48/85 | | 10/33 | 0/3 | 33/42 | 5/6 | | 0/1 |
| Corscaden & Tovell[13] | 1938-48 | 1954 | 134/251 | | 13/57 | | 87/127 | 34/62 | | |
| Cosbie[8] | 1937-47 | 1954 | 108/234 | 30/100 | | | 35/59 | 43/68 | | |
| Waterman et al.[7] | 1936-45 | 1952 | 72/126 | | 12/28 | | 41/67 | 15/22 | | |
| McKelvey et al.[20] | 1939-46 | 1952 | 89/154 | 1/7 | 11/26 | | 61/80 | 16/24 | | 0/17 |
| McKelvey & Tompkins[4] | 1947-49 | 1955 | 28/36 571/1033(55%) | 31/107(29%) | 49/162(30%) | 0/3 | 261/379(69%) | /32 189/285(66%) | | 9/41 |
| Kottmeier[21] | 1936-45 | 1955 | 638/1032(62%) 1313/2224(60%) | | 428/695(62%) | | | | | |

*Cure defined as all patients living & well, with no evidence of disease 5 yr. after treatment & rate expressed as no. cured per no. seen or treated.

figure from the clinics employing both methods, where the material is more likely to be similar. It is well to recall that even the Swedish series is not exclusively the result of radiotherapy, for in 13 per cent of cases treated initially with radium signs of recurrence subsequently developed, and hysterectomy was performed. Sixty-two per cent of these patients went on to live for five years.

## PREOPERATIVE RADIATION COMBINED WITH HYSTERECTOMY

Surgeons doing hysterectomy for cancer of the uterine body were distressed by local recurrence in the vagina, pelvis or laparotomy incision and cast about for a better solution. The local recurrences were regarded as being due to spillage at the time of operation. Too frequently, grumous tumor was extruded from the cervix under traction or pressure applied above. Attempts to deal with this by preliminary suture of the cervix and ligation of tubes may have reduced the wound recurrence, but had done. At the time of removal, as many as two thirds of the patients[24] showed no tumor in the specimen. There are remarkably few data on the reduction of local recurrence by this means. Recurrence in the vagina occurs in about 11 per cent of cases.[11]

An advantage of preliminary radiation recently emphasized by Corscaden and Tovell[13] is the reduction in size of the large, bulky tumor and uterus, thus facilitating hysterectomy. Undoubtedly, this increases the operability rate, not only by the technical advantage of shrinking the tumor but also by holding it in check long enough for the general preparation of the patient — that is, reduction of obesity and correction of cardiac failure or debility. There are two major disadvantages of preoperative radiation. One is that it is expensive in time and money, and the other that some patients whose symptoms have been relieved by the radiation fail to return for the definitive treatment at the appointed time and thus lose their best chance of cure. Attempts to deal with these defects are inconclusive. Shortening of the

time between radium application and surgery has been suggested. Why not apply the radium and operate four days later, or even the next day? The theoretical objection is that radiotherapy exerts its effect slowly. The tumor damage only partly derives from direct impact of the rays; the remaining and probably critical effect is by way of the adjacent normal tissues. This is a process that reaches its maximum intensity in about two weeks, and gradually declines over the following weeks. Heavily irradiated only. With this procedure a fat cylinder, 2.5 cm. in diameter and containing radium, is inserted in the vagina. The total dosage in milligram hours varies with the length of the applicator but is roughly 1000 milligram hours, a dose of 2000 $r_g$ 1 cm. beneath the vaginal surface. Of great importance is an applicator of the proper length so that the entire length of vagina from apex to urethral meatus is irradiated, for metastases are especially apt to occur adjacent to the urethra at the introitus and at the apex. The dis-

TABLE 4. *Primary Mortality of Treatment* and Five-Year Cure Rate According to Treatment and Clinical Stage (Present Series).*

| CLINICAL STAGE | HYSTERECTOMY ALONE | | | PREOPERATIVE RADIATION & HYSTERECTOMY | | | RADICAL HYSTERECTOMY & REGIONAL LYMPHADENECTOMY† | | |
|---|---|---|---|---|---|---|---|---|---|
| | NO. OF CASES | DEATHS | CURES | NO. OF CASES | DEATHS | CURES | NO. OF CASES | DEATHS | CURES |
| Stage 1, Group 1: | | | | | | | | | |
| 1927-37 | 79 | 5(6%) | 47(60%) | 8 | 1 | 4 | 0 | | 0 |
| 1938-50 | 103 | 3(3%) | 72(70%) | 135 | 6(4%) | 87(64%) | 24 | 2(8%) | 15(62%) |
| Stage 1, Group 2: | | | | | | | | | |
| 1927-50 | | | | 7 | 1 | 4 | | | |
| Stage 2: | | | | | | | | | |
| 1927-50 | 1 | 0 | 0 | 3 | 0 | 1 | | | |
| Totals | 183 | 8(4%) | 119(65%) | 153 | 8(5%) | 96(63%) | 24 | 2(8%) | 15(62%) |

*Death within 30 days of treatment.
†14 of these had no preoperative radiation, & 8 cured; 10 had preoperative radiation, & 7 cured; 2 had positive lymph nodes, & neither lived 5 yr.
‡Some of these treated at other institutions.

animal tumor will flourish if promptly transplanted to an unirradiated site.[25] Thus, early operation shortly after irradiation may rob the procedure of its essence. Surgery in less than two weeks is inadvisable, and three to six weeks after irradiation is probably the optimum time. If one is to apply preoperative radiation, it is probably best done with multiple sources such as the Heyman capsules, with a dose in the average-sized uterus of about 2000 milligram hours and a vaginal application of 1000 milligram hours in a cylinder 2.5 cm. in diameter. This would deliver roughly 2000 gamma r to the peritoneal surface of the uterus and to the vagina 1 cm. beneath the surface.

The available figures on immediate mortality of preoperative radiation and hysterectomy are limited, but they suggest a risk comparable to that of primary hysterectomy, and actually the 2 deaths out of 303 cases, or 1 per cent mortality, is the lowest in the collected figures (Table 2). The cure rate of this procedure (Table 3) is 69 per cent, which, although slightly superior to that of hysterectomy alone, is not significantly so.

Postoperative radiation also has been proposed to prevent local recurrence. Full-pelvis x-ray therapy seems excessively expensive (a mid-pelvic dose of 3000 r given over a period of three weeks), especially since there is no proof of its value in this situation. The most attractive plan for postoperative radiation is that of Kottmeier, which involves vaginal radium advantage of this procedure is that it is best given three to six weeks after operation, thus requiring a second hospital admission. Irradiation immediately after operation may interfere with healing. The advantage of the method is the ease of application and the brief hospital stay (two or three days). Kottmeier[21] reported that only 4 of 172 patients treated in this manner manifested vaginal recurrence in two to three years of follow-up study — a rate of 2.3 per cent. Thus, the frequency of recurrence is reduced to a third of that expected, which is probably worth while.

## RADICAL HYSTERECTOMY

In the last few years there has been a renaissance of radical hysterectomy for cancer of the cervix and, understandably, an attempt to apply it to lesions of the uterine body as well. There is no unanimity regarding the inclusion of regional lymphadenectomy with this procedure.

Experience has shown that operable carcinoma of the corpus has regional-lymph-node involvement about as frequently as cancer of the cervix — that is, 21 per cent. In a series of 228 cases of carcinoma of the corpus collected from the literature,[10,11,15,26-28] the lymph nodes were positive in 47 (21 per cent). This is the same frequency observed in a larger collected series of cancer of the cervix.[29] The regional lymph nodes tend to be involved more frequently if the

lesion has extended to the endocervix.[28] Lymphadenectomy has been advocated and is being practiced with increasing frequency. A formidable obstacle to the application of radical hysterectomy and regional lymphadenectomy is the general condition of the patient with carcinoma of the corpus. She tends to be fat, diabetic and hypertensive, and a decade older than the one with a lesion of the cervix. Inevitably, this leads to a high morbidity and mortality in even the most experienced hands.

nificant figure in the literature, although a number of other series are now being followed. Forty-five of Winterton's patients lived for five years — a 79 per cent cure rate, which is very good indeed. However, the element of preselection makes it difficult to know what margin of advantage the procedure really has over less extensive surgery or, indeed, over radiation alone. It should be noted that dissection of the regional lymph nodes was done in 28 of 90 cases, and in only 2 were there metastases.

TABLE 4 *(Concluded).*

| CLINICAL STAGE | RADIATION ALONE | | | TOTAL TREATED | | | NO TREATMENT | |
|---|---|---|---|---|---|---|---|---|
| | NO. OF CASES | DEATHS | CURES | NO. OF CASES | DEATHS | CURES | NO. OF CASES | CURES |
| Stage 1, Group 1: | | | | | | | | |
| 1927-37 | 8 | 0 | 2 | 95 | 6(6%) | 53(56%) | 9 | 5‡ |
| 1938-50 | 16 | 0 | 7 | 278 | 11(4%) | 181(66%) | 2 | 0 |
| Stage 1, Group 2: | | | | | | | | |
| 1927-50 | 72 | 2(3%) | 33(46%) | 79 | 3(4%) | 37(47%) | 5 | 0 |
| Stage 2: | | | | | | | | |
| 1927-50 | 28 | 2(7%) | 3(11%) | 32 | 2(6%) | 4(12%) | 18 | 0 |
| Totals | 124 | 4(3%) | 45(36%) | 484 | 22(5%) | 275(57%) | 34 | 5 |

*Death within 30 days of treatment.
†14 of these had no preoperative radiation, & 8 cured; 10 had preoperative radiation, & 7 cured; 2 had positive lymph nodes, & neither lived 5 yr.
‡Some of these treated at other institutions.

Radical hysterectomy combined with regional lymphadenectomy has a restricted field of application. In the present material of 80 patients operated on in the four-year period, from 1947 to 1950, inclusive, there were 24 radical hysterectomies. Admittedly, no great effort was made to apply the radical procedure to all cases, but this was a period of extending the operative indications. Brunschwig and Murphy[15] estimate that they have performed radical lymph-node excision in 20 to 25 per cent of their patients operated on since 1947. They add that it is their intention to use the procedure more often in the future. The frequency of election of radical hysterectomy and regional lymphadenectomy will depend upon the enthusiasm of the operator and the type of procedure he employs, as well as the type of case he is presented with. There is a wide range in the extent of dissection and tissue removed from clinic to clinic and, indeed, from case to case. Brunschwig and Murphy indicate that they employ a less radical procedure in cancer of the corpus than in carcinoma of the cervix. Winterton[10] reports the astonishingly high operability rate of 95 per cent in 90 cases over the past twelve years.

The risk of radical hysterectomy is minimal if the published figures are to be accepted at face value, for a 3 per cent operative mortality (5 deaths among 164 patients) is low.

The results of radical hysterectomy are indicated by Winterton's series of 57 cases. It is the only sig-

## GENERAL CONSIDERATIONS

From this survey, one can conclude that all the methods of treatment are effective. Operability, primary mortality and five-year cure are the product of a number of factors. These variables are too numerous and too subtle to allow an entirely satisfactory evaluation of the published statistics. I am aware of no series in which all the cases from a given geographic area are included. The bulk of patients with carcinoma of the corpus are first seen by their own physicians, who tend to operate on patients with the most favorable cases themselves or to refer them to a clinic strong in surgery, whereas patients with advanced cases are generally sent to radiotherapy units. Thus, by preselection, one clinic may have a high operability rate, a low primary mortality and a high five-year cure whereas the reverse is true of another clinic, even though its treatment is equally effective.

Because of the several available procedures, selection of the method of treatment is employed in almost all clinics. If all four of the types of treatment mentioned are equally available, there is a tendency to elect radical hysterectomy for the most favorable, hysterectomy for the patient who is not quite so robust, preoperative radiotherapy followed by surgery for the one whose lesion is a little larger, and radiotherapy for the poor-risk patient with an advanced case. Obviously, this philosophy is not uniformly applied, but basically it tends to operate and to in-

fluence the results entirely apart from the skill with which the treatment is applied.

An analysis of the published statistics is thus inconclusive as a method of determining the best treatment for this disease. To compare the results of one clinic with those of another where the quality of the material, the criteria for selection and the mode of treatment are all different is of limited value. Another perspective is afforded by the experience of a single clinic where some of these variables are recognized, if not entirely controlled.

## Present Series

In the years 1927-1950, 518 patients with carcinoma of the uterine corpus were seen in the Vincent Memorial and Massachusetts General Hospital and at Pondville Hospital.* This material has been reviewed and assigned a clinical stage according to the description in the record. The limitations of this technic are obvious. No treatment was given to 34 patients (7 per cent). There were 484 treated cases. In the entire series, 384 (74 per cent) cases were classified as Stage 1, Group 1, 84 (16 per cent) as Stage 1, Group 2, and 50 (10 per cent) as Stage 2. A 57 per cent cure rate was obtained in all treated cases — that is, 276 of 484 cases. In Stage 1, Group 1, 235 of 373 (62 per cent) patients, in Stage 1, Group 2, 37 of 79 (47 per cent) patients, and in Stage 2, only 4 of 32 (12 per cent) patients were cured.

To compare the effectiveness of the various forms of treatment, only cases in Stage 1, Group 1, should be considered (Table 4), for these are the patients whom one could presumably treat with either surgery or radiation.

In addition, one should probably exclude patients treated before 1938 since preoperative radiotherapy was rarely used then and radical hysterectomy not at all.

Only 24 patients were treated with radical hysterectomy and regional lymphadenectomy, and of these, 15 had five-year cures. This is not statistically different from the cure rate in those treated by simple hysterectomy with or without preoperative irradiation, but it is certainly no better, and it is discouraging to note that both the patients with positive lymph nodes failed to survive.

The major value of these figures lies in the comparison that is possible between the patients treated by hysterectomy alone and those who received radiation before the extirpation. Most preoperative radiation was given with radium and preceded surgery by about six weeks. However, all cases in which irradiation was given within the three months before hysterectomy are defined as having received preoperative radiation. There is a tendency for more private patients to be treated by primary surgery and more clinic patients to be given preoperative radiation, which may favorably weigh the series in which surgery alone was given. Nevertheless, the two series are fairly comparable in that they consisted of cases in the same institutions, treated by the same staff, concurrently — a point that should be emphasized because it is difficult to evaluate the series that follow one another in time. Cases treated five years ago, when compared to those treated today, may only reflect the general improvement in medicine. The series presented here were accumulated at the same time, thus obviating that particular criticism.

Hysterectomy alone achieved a five-year cure rate of 70 per cent (72 of 103 cases), whereas preoperative radiation and hysterectomy resulted in a 64 per cent (87 of 135 cases) cure rate. These figures are little different, but suggest some modest advantage of hysterectomy alone that may be only the result of selection. The failure of preoperative irradiation to achieve a clear advantage is damaging to the routine use of that technic because the increased expense in time, money and discomfort can only be justified by a distinct improvement in the cure rate.

The risk of treatment, as might be expected, is least in patients treated radiologically (3 per cent), a shade higher in those with hysterectomy (4 per cent) and radiation combined with hysterectomy (5 per cent), and highest in those with radical hysterectomy (8 per cent).

## Discussion

From these data, it is evident that cancer of the uterine corpus can be effectively treated in several ways. Cases in Stage 1, Group 1, are treated effectively by the four methods discussed. Total hysterectomy is thus the treatment of choice because the risk is low and minimal time and discomfort are involved. Preoperative radiotherapy is indicated in the patient with a large lesion that could be removed more comfortably if reduced in bulk. It is also indicated in the marginal Group 2 case in which a few weeks or months of preparation would correct the obesity, cardiac failure and so forth that precluded primary operation and thus allow an ultimate hysterectomy. Radiotherapy can be used in the operable case if equal facilities for hysterectomy are not at hand. The prophylactic use of radium in the vagina after hysterectomy seems worth while to diminish recurrence there.

Radical hysterectomy for this disease must be considered an experimental procedure that remains to be proved, for a clear advantage in cure rate needs to be evident to offset the inevitably higher morbidity and mortality.

Radiotherapy is the treatment of choice for all cases

*290 at Vincent Memorial and Massachusetts General Hospital; 228 at Pondville Hospital.

not suitable for total hysterectomy. However, any patient in whom bleeding, pyometrium or an enlarging uterine mass develops after irradiation should be re-evaluated for hysterectomy if possible, for these cases represent probable recurrence, and the subsequent survival rate is good if uterine removal is possible.

## Summary and Conclusions

Four methods of treatment of cancer of the uterine corpus are reviewed — that is, total hysterectomy, with or without preoperative radiation, radiotherapy alone and radical hysterectomy with regional lymphadenectomy. The applicability, mortality rates and cure rates of series in the literature and in the present series are discussed.

Total hysterectomy alone is the procedure of choice. The risk of vaginal recurrence can be reduced by the use of postoperative radium. There are special indications for preoperative radiation and for radiotherapy alone.

I am indebted to Miss E. Patricia Wolfson for her help in the compilation of data in the "present series."

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# EXPERIENCE WITH THE USE OF CHLORPROMAZINE AND RESERPINE IN PSYCHIATRY

## With Especial Reference to the Significance and Management of Extrapyramidal Dysfunction

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THE introduction of the tranquilizing or ataraxic drugs in the treatment of mental illness during 1954 resulted in widespread research in the use of these agents and numerous publications of the findings. Varying results have been obtained, and diverse programs for administration have been suggested. Despite differences in dosage ranges and duration of therapies, most practitioners who have used the ataraxics recognize their role in providing symptomatic relief in many types of psychiatric disorders and in facilitating the introduction of adjunctive therapies and the management of patients. Some practitioners believe that the drugs have brought about or helped bring about interruption or alteration of basic psychotic processes, particularly in schizophrenia. The ataraxics, depressants of the central and autonomic nervous systems, appear to act chiefly on subcortical areas of the brain. To these agents, many clinicians have added milder stimulants to overcome concomitant therapeutic effects or side reactions.

Although ataraxics had been in use at the Vermont State Hospital since May, 1954, they were not used extensively until early September of the same year.

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All told, 386 female patients began treatment with ataraxics before September 1, 1955. This report concerns the experience with this group through January 11, 1956, and represents over 40 per cent of the total number of female patients treated during the period of study. During the early months of this study most patients were selected because they presented some problem of disturbed behavior. However, as experience increased, the group was expanded to include a number of nondisturbed patients of various types.

mg. of chlorpromazine or 3 mg. of reserpine, or in combination, 150 mg. of chlorpromazine and 1 mg. of reserpine. Not more than 800 mg. of chlorpromazine or 30 mg. of reserpine or 450 mg. of chlorpromazine and 3 mg. of reserpine were given in one day.

The duration of treatment has ranged from one to sixteen months. It is planned to continue treatment indefinitely for a number of patients with more chronic disorders. In 204 of 386 patients at least minimum signs of extrapyramidal disorder were de-

TABLE 1. *Status of Patients on January 11, 1956, by Diagnostic Group.*

| DIAGNOSIS | TOTALS | PATIENTS RELEASED | | PATIENTS VERY MUCH IMPROVED IN HOSPITAL | PATIENTS MUCH IMPROVED IN HOSPITAL | PATIENTS MODERATELY IMPROVED IN HOSPITAL | PATIENTS NOT IMPROVED | PATIENTS FOR WHOM DRUGS STOPPED | PATIENTS WHO DIED |
|---|---|---|---|---|---|---|---|---|---|
| | | OFF DRUGS | ON DRUGS | | | | | | |
| Schizophrenia: | | | | | | | | | |
| >5 yr. in duration | 176 | 13 | 29 | 12 | 61 | 46 | 3 | 8 | 4 |
| <5 yr. in duration | 50 | 29 | 11 | 2 | 5 | 0 | 0 | 1 | 2 |
| Manic reaction: | | | | | | | | | |
| >5 yr. in duration | 8 | 0 | 1 | 0 | 2 | 3 | 0 | 2 | 0 |
| <5 yr. in duration | 22 | 19 | 1 | 1 | 0 | 0 | 0 | 0 | 1 |
| Psychoneurosis | 17 | 9 | 6 | 0 | 1 | 0 | 1 | 0 | 0 |
| Personality disorders | 11 | 11 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Acute brain syndrome | 5 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Chronic brain syndrome | 55 | 0 | 0 | 0 | 8 | 16 | 1 | 13 | 17 |
| Epilepsy | 8 | 0 | 2 | 0 | 2 | 3 | 1 | 0 | 0 |
| Mental deficiencies | 13 | 0 | 0 | 0 | 5 | 4 | 0 | 4 | 0 |
| Depressions: | | | | | | | | | |
| With electroconvulsive treatment | 14 | 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Without electroconvulsive treatment | 7 | 0 | 1 | 0 | 1 | 3 | 0 | 2 | 0 |
| Totals | 386 | 100 | 51 | 15 | 85 | 75 | 6 | 30 | 24 |

## MATERIALS AND METHODS

Of these 386 patients, 187 received chiefly chlorpromazine*, 67 chiefly reserpine,† and 132 a combination of the two. Since these drugs were administered at an early stage of their research, it was necessary to use imagination and courage in the regimens and vigilance in following the patients. The use of such medications as trihexyphenidyl (Artane), methyl-phenidylacetate,‡ mephenesin,§ benzotropine methanesulfonate (Cogentin), diphenhydramine (Benadryl) and thonzylamine (Neohetramine) to control side effects of the ataraxics required that the drug combinations or dosages be changed as often as 20 to 25 times in many patients. As a result, the figures on dosage regimens do not easily lend themselves to statistical evaluation.

The usual daily dosages for the ataraxics were 300

*Kindly supplied as Thorazine by Smith, Kline and French Laboratories, Philadelphia, to initiate this study.

†Kindly supplied as Serpasil by Ciba Pharmaceutical Products, Incorporated, Summit, New Jersey, to initiate this study.

‡Kindly supplied as Ritalin by Ciba Pharmaceutical Products.

§Kindly supplied as Mephate by A. H. Robins Company, Incorporated, Richmond, Virginia.

tected; this reaction is discussed below. To counteract it, trihexyphenidyl, 5 to 15 mg. daily, in 151 cases, or methyl-phenidylacetate, a new drug not yet on the market, 30 to 120 mg. daily, in 27 cases, or a combination of the two, in 26 cases, was added to the dosage of ataraxics.

## RESULTS

The over-all results are summarized in Table 1. It is evident that varieties of acute reactions respond most readily to these drugs. They do not seem to be of dramatic value in chronic reactions except in schizophrenic and paranoid reactions, or psychoneurotic and personality disorders with anxiety. Of patients with schizophrenic or paranoid psychoses who were ill for five years or longer, 164 were able to continue a course of treatment. Forty-two have been discharged. Of these, 10 had had deep insulin-coma treatments, and most others had had one or more courses of electroconvulsive therapy. Twelve, still in the hospital, are very much improved and expected to go home soon. Sixty-one are much improved, to the point of enjoying social activities and

engaging in useful occupations. Forty-six are improved in the sense that they are quiet, tractable and co-operative with ward routine. Only 3 are unimproved. As in other treatment programs, paranoid and catatonic schizophrenias responded somewhat more readily than other types.

There were 50 patients with schizophrenic or paranoid reactions who had been ill for less than five years. Of these, 40 are now out of the hospital, another 2 are very much improved and about ready to leave, and 5 are much improved.

Fifty-five patients suffering from chronic brain syndrome* have responded less favorably. None have been discharged, only 8 are much improved, 13 have had to be taken off the drugs, and 17 have died.

These drugs seem to be specific for acute manic reactions. The results with chronic manic reactions have been disappointing.

The ataraxics were of considerable value in controlling anxiety, agitation and acute delirious reactions accompanying electroconvulsive treatment of depressions.

The administration of chlorpromazine or reserpine or both is the treatment of choice in schizophrenic or paranoid reactions, in psychoneurotic or personality disorders with anxiety and in acute brain syndromes. In these cases 50 per cent of patients able to continue treatment have been discharged. Another 31 per cent are much or very much improved. Of patients with these disorders who have been mentally ill for less than five years, 80 per cent have been discharged, and an additional 9 per cent are much improved.

Of the 151 patients now in the community, 90 have been out of the hospital for more than six months, and 122 for more than four months. The remaining 29 have been released during the past four months.

Of the 151 patients who have been released from the hospital, 109 received chiefly chlorpromazine, 15 were treated with reserpine alone, and 27 with a combination of the two.

In this series, 24 patients died during the course of the study, but this represents no significant change in either the death rate or the pattern of causes in the female service. There is no indication, in 23 of these cases, that death was connected in any way with the use of the medications. Only 15 of these patients had received ataraxics during the two weeks before their terminal illness. Of the 24, 17 were over seventy years of age, 13 being over eighty. Seventeen of the group suffered from chronic brain syndromes. The chief causes of death were respiratory and circulatory: 10 died of bronchopneumonia, 5 of circulatory disturbances, and 2 of cerebrovascular accidents. One patient died of perforated duodenal ulcer a day after beginning to receive 3 mg. of reserpine daily.

The usually reported side effects of the ataraxics were encountered in this study. In the group taking chlorpromazine, a variety of rashes developed in 48; 2 of these were severe exfoliative dermatitis, which occurred before those administering treatment were alert to this possibility. Thereafter, the administration of antihistaminics for two or three weeks controlled all these skin disorders, usually without reduction in the dose of chlorpromazine. In 3 patients mild leukopenic reactions developed on chlorpromazine therapy; 2 were continued on the drug with satisfactory increase in blood counts, and 1 was shifted to reserpine. There were 3 cases of jaundice with chlorpromazine, but 1 patient has been receiving the drug again for six months without signs of recurrence. Among the patients on reserpine, 15 had gastritis with anorexia and some nausea and vomiting. In 4 patients taking trihexyphenidyl a toxic delirium occurred, subsiding within a day or two of withdrawal of the drug or reduction of dosage. Five patients had a return of excited behavior with methyl-phenidyl-acetate.

*The terms "acute" and "chronic" brain syndrome follow the official classification adopted by the American Psychiatric Association in 1950.

## Discussion

The results of the study are more impressive in terms of qualitative improvements in the patients and in hospital routine than in those of quantitative or statistical analysis of this experience. Particularly impressive has been the striking facilitation of communication with patients with chronic schizophrenia. Even before the patients began to lose their hallucinations and bizarre ideation, it became possible to talk directly with the person behind the disease. As the malignant mental trends began to fade, a peculiar type of objectivity and insight, such as had not been seen before, developed. The patients were able to talk about their strange experiences in the way normal people recount bad dreams. After the hallucinations had disappeared, several patients referred to them in words similar to these: "It's hard to describe what it's like to be insane — it's something like being in a bad nightmare all the time."

One of the most encouraging results has been the release from the hospital of the 42 patients with severe schizophrenic or paranoid reactions that had lasted for more than five years. Twenty-four have been out for more than six months. Seventeen had been suffering from mental illness for over ten years, 1 for twenty years, and 1 for thirty years. Twenty-nine of these patients have been continued on medication outside the hospital. Thirty-five are productive members of the community. Five are making a marginal adjustment. Only 2 have relapsed at home and may be returned to the hospital soon. These patients were treated for two to ten months before they were able to leave the hospital. Most required four to six months of treatment. Of these patients, 23 received chlorpromazine, 6 reserpine, and 13 a combination of the two.

The detection of extrapyramidal dysfunction in 204 patients has led to two interesting observations.

In the first place the initial sign of improvement often coincides with the onset of obvious extrapyramidal disorder. This onset varied from four weeks to four months in patients receiving only one of the ataraxics, but tended to occur in two to four weeks in those receiving a combination of the two drugs. Before a more extensive and detailed survey of patients for this reaction was made, obvious signs had been noted in 18 per cent of those on reserpine, 30 per cent of those on chlorpromazine, and 56 per cent of those on the combination. The other observation was that the patient's immediate progress was enhanced when extrapyramidal dysfunction was relieved. Slowness of motion, loss of some associated movements, loss of facial mobility and some cogwheel rigidity were regarded as minimum signs. These were relieved by the addition of trihexyphenidyl or methyl-phenidylacetate or both to the regimen. The patients' muscles loosened up, they complained less of lameness and fatigue, their mood improved, and they more readily participated in re-education efforts. After a number of other medications had been tried, trihexyphenidyl was added for 151, methyl-phenidylacetate for 27, and both for 26 patients. Of 232 patients still on ataraxics, 80 per cent are receiving these drugs as well.

Before the occurrence of extrapyramidal signs became a consideration, many patients had left the hospital; however, of the 181 still under medication in the hospital, 89 per cent showed some dysfunction. A variety of disorders developed, including 3 cataleptic states with a suggestion of oculogyric crises, 2 cases of spasmodic torticollis, a number of cases of extreme restlessness, with constant aimless motions suggestive of chorea, and many cases of sialorrhea. All responded favorably to the addition of trihexyphenidyl or methyl-phenidylacetate, or a combination of the two, to the medication schedule. In a few cases it was also necessary to reduce the dose of ataraxics. It was believed that careful attention to the management of extrapyramidal dysfunction contributed greatly to the progress of many patients.

As far as I know, only one other investigator, Haase,[1,2] has reported a comparable occurrence of extrapyramidal dysfunction among patients treated with large doses of ataraxics. He reported signs and symptoms of Parkinsonism in 88 per cent of his patients. In his series this effect was carefully studied by extensive analysis of changes in handwriting. He postulated that the changes in extrapyramidal function are the essential effect ("Eigenwirkung") of the drugs on the central nervous system. My opinion has been that signs of Parkinsonism heralded the particular effect being sought. However, it was found that the therapeutic effects were not dependent on extrapyramidal dysfunction. On the contrary, alleviation of such dysfunction, as soon as it occurred, sped the progress of recovery.

Although, as noted above, most of the 386 patients in this study had presented considerable problems in behavior, a few were very withdrawn, quiet, seemingly "comfortable" patients with schizophrenia. Some of these chronically ill patients did not show any great improvement until as much as six months after the beginning of the treatment. It has been believed that a trial of treatment lasting less than six months would be inadequate for any chronic, severe psychotic condition.

The qualitative changes wrought in mental-hospital practice have been impressive. The disturbed wards no longer deserve the name. Restraints and seclusion have been practically abolished. Departments of recreational, occupational and industrial therapy have been strained to the utmost to provide for the vastly increasing number of patients who are able to participate in these activities. Destruction of clothing and bedding has been greatly reduced. Many patients who had not been properly dressed in years are now neat and clean. The wards smell better. The atmosphere in those for "deteriorated" and "disturbed" patients at mealtime is strikingly changed; meals are now a comparatively quiet, pleasant interlude.

A total of 51 patients in this series have continued receiving medications outside the hospital. The majority of these return to the hospital at least once a week at first, for an interview and a prescription or a supply of medicine for a state-supported patient. A few have been followed primarily by their own physicians or private psychiatrists.

The most pressing problem for the future is the rehabilitation of the 73 much improved patients with chronic schizophrenic or paranoid disorders that had lasted for more than five years. Many in this group have lost all contact with the community. A few have been divorced as "incurably" insane. The families of some have died, or drifted away. A small beginning in a co-operative program with the Division of Vocational Rehabilitation has been made. Jobs have been found for 3; the Division of Vocational Rehabilitation is working with 6 others who are out of the hospital and 16 others who are still inside. It is recognized that there is a need for a far more ambitious, extensive and imaginative program of research in comprehensive public-health medicine, in co-operation with the Division of Vocational Rehabilitation, mental-health clinics and other agencies under the direction of the University of Vermont College of Medicine, to study community resources and attitudes and search for the most effective methods to fit these people back into productive life in the community.

## Summary

Chlorpromazine, reserpine and a combination of these two agents (in a ratio of 150 mg. of chlorpromazine to 1 mg. of reserpine) have been employed

as standard medications in 386 psychotic female patients for a period of sixteen months at Vermont State Hospital. Most of these patients were agitated or showed antagonistic attitudes. A number of antidepressant drugs, particularly trihexyphenidyl and methyl-phenidylacetate, have been added to the dosage regimens of many patients to control side effects of the ataraxics.

One hundred and fifty-one patients have been discharged; 15 others are awaiting discharge; 85 are much improved, though still in the hospital; and 75 are improved, being quiet and co-operative with ward routine.

Qualitative improvement in many psychoses was likewise impressive. The drugs appeared to facilitate communication with patients with chronic schizophrenia. A peculiar type of objectivity and constructive insight was noted in many cases. In this series 36 patients failed to respond to treatment or had to be taken off the drugs, and 24 died during this period. The death rate was normal in comparison with that in previous years.

The occurrence of extrapyramidal dysfunction was usually followed by initial signs of improvement in the patient's psychosis. The chlorpromazine-reserpine combination tended to produce this dysfunction more frequently and sooner than either drug alone. The patient's progress was enhanced when this dysfunction was relieved by trihexyphenidyl or methylphenidylacetate, which are now in use for this purpose in 80 per cent of the drug-treated patients.

Conditions within the hospital have been significantly improved: disturbed wards have been virtually eliminated; the atmosphere of dining halls and living areas has been transformed; and psychotherapeutic and sociotherapeutic facilities are being widely utilized. These results emphasize the need for social agencies to help the hospital restore to society patients like the 73 who are being retained largely because their families can no longer absorb them after five years or more of mental illness.

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# HEREDITARY HEMATURIA, NEPHROPATHY AND DEAFNESS*

## Preliminary Report

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THIS report is concerned with a familial renal disease associated with nerve deafness. Familial renal disease without associated nerve deafness, which has been adequately reviewed by Eason,[1] Rinkoff[2] and Reyersbach[3] and their associates, is not discussed further here.

We are of the opinion that the three following criteria are necessary for the diagnosis of this syndrome: a family history of progressive renal disease in males affected; the presence or history of hematuria, which may be intermittent; and nerve deafness in most of the males and in some of the females affected. We have thus termed this entity "hereditary hematuria, nephropathy and deafness," which describes the essential characteristics of the disease. We present the following brief report of a typical case.

### Report of Case

A 7-year-old boy was admitted to the Mayo Clinic on September 14, 1954, because of hematuria. Ten weeks previously he had noticed that his urine was dark. Examination of the urine by his physician had revealed the presence of many red blood cells. A diagnosis of acute glomerulonephritis had been made, and the boy had been placed at rest in bed. Eight weeks before admission to the clinic he had been allowed out of bed. Urinalysis again showed many red blood cells and a positive reaction for albumin. The value for nonprotein nitrogen in the serum was 38 mg. per 100 ml. Two weeks later he was examined by a urologist. At that time the blood pressure was 90/60. The urine had a specific gravity of 1.022 and gave a +++ test for albumin, and the sediment contained many red blood cells but no casts. Four weeks before admission an excretory urogram revealed a "complete duplication of the left pelvis and ureter and a mild ureteropelvic cut-off on the right, with some haziness of the calyceal outline." Specimens of urine collected over a 24-hour period were examined for tubercle bacilli, with negative results. Two weeks later the blood pressure was 98/60, and the erythrocyte sedimentation rate was normal; the urine gave a +++ test for albumin, and the sediment contained many red blood cells and a few hyaline and granular casts.

The family history (Fig. 1) revealed that the patient's mother had had frequent bouts of hematuria. One of the mother's sisters had had occasional episodes of hematuria and had been deaf since childhood. Her family physician had been unable to find a cause for the hematuria. Another of the mother's sisters had died at 30 years of age of "uremic poisoning" after pregnancy. Two of the mother's brothers had died at the ages of 26 years and 19 years of chronic nephritis; both had been deaf since their early teens. The older of the 2 had been confined to a hospital during his last illness. He had been stuporous and had had convulsions.

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The value for urea was 674 mg. per 100 ml. of blood. Autopsy was not carried out. The patient's maternal grandmother had had hematuria intermittently throughout her life. Three of the grandmother's brothers had died before the age of 30 years of Bright's disease or uremia; all were deaf. A cousin, who had died at the age of 23 years of Bright's disease, was known to have been deaf. Another cousin, a 13-year-old boy, had chronic nephritis, which had been discovered when he was 9 years of age; he had been partially deaf since he was 5, with "57 per cent loss in the right ear and 26 per cent in the left."

Physical examination did not reveal abnormalities aside from loss of hearing.

Letters from the mother in November, 1954, and August, 1955, reported that laboratory tests continued to show red blood cells, casts and albumin in the urine. The patient was feeling well and had been attending school.

## Discussion

In 1902 Guthrie[4] described a family in which 12 members had hematuria. He noted that the hematuria was gross in some members and microscopic in others. Febrile illnesses were said to increase the amount of blood in the urine. In some of the members the ingestion of black currants aggravated the hematuria. Evidence of nephritis was not found.

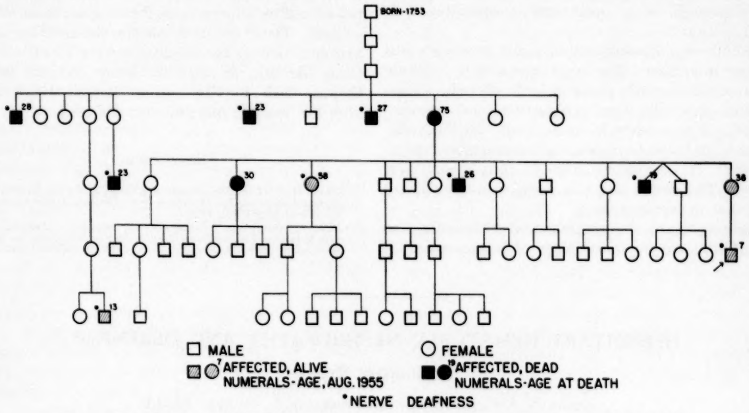


FIGURE 1. *Occurrence of Hereditary Hematuria, Nephropathy and Deafness in One Family. The arrow points to the proband.*

The value for urea was 28 mg. per 100 ml. of blood. The results of repeated urinalyses revealed persistent albuminuria and hematuria associated with a few granular and blood casts in the sediment. Electrophoretic studies of the serum gave the following results: albumin, 50 per cent; alpha-1 globulin, 6 per cent; alpha-2 globulin, 17 per cent; beta globulin, 18 per cent; gamma globulin, 9 per cent.

An audiogram disclosed bilateral, partial nerve deafness, the greatest loss being for tones in the range of 500 to 4000 vibrations per second. The loss was approximately equal bilaterally and measured 30 to 50 decibels. It is of interest that deafness was not a major complaint. The audiogram was done out of curiosity to see if the patient did have nerve deafness.

In consultation with the urologists it was decided that cystoscopy under anesthesia should be carried out. During this examination the bladder and ureteral orifices were observed to be normal. The right ureter was catheterized, and a pyelogram showed the calyxes to be blunted and dilated. Specimens of urine from the right ureter and bladder when stained by the Gram method did not show any organisms.

The urologists were of the opinion that this boy had pyelonephritis, though the pediatricians were inclined to favor chronic nephritis. It was decided that he should not participate in any activities except school and that he should take 250,000 units of penicillin by mouth daily. A prescription was given for 3,4-dimethyl-5-sulfanilamidoisoxazole (Gantrisin), 1 teaspoonful 3 times daily for the 1st week of each month. It was suggested that urinalyses be done every 2 weeks. The patient was dismissed from the hospital on September 21.

Kendall and Hertz,[5] Hurst[6] and Alport[7] reinvestigated the family reported by Guthrie.[4] These authors added a few cases and re-evaluated the cases previously reported. Kendall and Hertz[5] observed that in these cases hematuria was often intermittent but that albuminuria persisted. Seven males and 8 females were afflicted with the disease. In the males the disease was characterized by the presence of hematuria, albuminuria, cylindruria and nerve deafness usually, and by death from chronic renal disease before the patient was twenty years of age. Two males were alive at thirteen and fifteen years although they had the disease. In the females the disease was characterized by the presence of hematuria, albuminuria, cylindruria and occasional nerve deafness, a chronic course and a relatively good prognosis. Two of the three females in the first generation who did not have renal disease were said by Alport[7] to be deaf.

Although four authors studied this family over a twenty-five-year period, only Alport[7] discussed the

nerve deafness. The 3 afflicted males who were not known to be deaf had not been studied for deafness.

Reyersbach and Butler[3] recently described a family in which they found 22 cases of renal disease with nerve deafness. In the males the disease was characterized by albuminuria with minimal hematuria and cylindruria, nerve deafness, usually, and progressive renal disease causing death at an early age. In the females the disease was characterized by albuminuria with minimal hematuria and cylindruria, occasional nerve deafness and a tendency to hypertension, toxemia and edema during pregnancy. The females generally had a normal life span. Fifteen males and 7 females had the disease. Four males had congenital eye defects.

It appears that the families studied by Guthrie[4] and by Reyersbach and Butler,[3] and by us, are the only ones with hereditary hematuria, nephropathy and deafness. These 3 families are all of Anglo-Saxon origin. We have traced the kindred of our patient back six generations to his great-great-great-grandfather, who was born in Ireland in 1753 of English parentage. The possibility exists, therefore, that this family is related to the families studied by Guthrie and Reyersbach and Butler.

So far as the disease is concerned, our patient's relatives present a background strikingly similar to the backgrounds of the other 2 families. As pointed out previously, in our case the child has albuminuria associated with hematuria, cylindruria and nerve deafness; 6 males in the patient's family, all of whom were known to be deaf, died of renal disease at an early age; 1 other male relative, thirteen years of age, has chronic renal disease associated with deafness; the majority of females affected have had a relatively benign course; 1 female is deaf, and hematuria has been intermittent in some members of this family.

Reyersbach and Butler[3] mentioned 3 other families in which they found a total of 6 cases of "congenital hereditary hematuria." One patient, an only child, did not have nerve deafness, and renal disease was not mentioned in the family history. In another family 3 female siblings who had hematuria were not deaf; their mother had albuminuria and hypertension. However, no other case of nerve deafness or renal disease was presented in the family history. In the third family, 2 members were afflicted with nerve deafness but did not give a family history of renal disease. From these limited data we cannot say that any of these 6 patients had hereditary hematuria, nephropathy and deafness.

Mamou and Cattan[8] investigated a family, of Jewish extraction, in which 7 members had renal disease; several members also had periodic attacks of peritonitis. Four females died of renal disease at the ages of twenty-four, nineteen, seventeen and thirteen years. One man, twenty-five years of age at the time of the report, had chronic nephritis. Another male had been deaf since the age of twelve years; he had also had albuminuria since childhood. No other cases of deafness were mentioned. Since the report was primarily concerned with periodic peritonitis, data were insufficient to evaluate the family for hereditary hematuria, nephropathy and deafness. Moreover, the fatal outcome in 4 of 5 female patients is against such a diagnosis.

Perkoff et al.[9] described a family "in which 50 members have renal disease with the characteristics of chronic interstitial pyelonephritis but in which progressive renal insufficiency develops only in the males." Eight males had died of the disease. Autopsy in 3 of the 8 cases showed that the patients had had chronic interstitial pyelonephritis. Six of the 8 had had nerve deafness. The urine of 44 of the members of the family was examined; proteinuria and pyuria were the major abnormalities, although the urine of 5 members contained pathogenic bacteria. Fourteen persons in this family were deaf. These authors concluded that "the nephritis in this kindred is related to the transmission of an incompletely sex-linked dominant gene." This disease is set apart from hereditary hematuria, nephropathy and deafness by pyuria and the pathologic finding of pyelonephritis.

Sohar[10] recently investigated 10 members of a Jewish family in Israel. The mother of 7 children is deaf, and her urine contains albumin and casts. Each of her 4 sons, eighteen, seventeen, sixteen and fourteen years of age, has albuminuria with minimal hematuria; in addition all have considerable inner-ear deafness, with positive recruitment. Two of the boys have spherophakia; the other 2 have congenital posterior cataracts. A sister, aged nine years, has albuminuria and cylindruria, but she was not examined further. Two other sisters were not examined. Two maternal uncles, who had died in Iraq of renal failure at twenty-two and twenty-four years of age, had also been deaf.

This information strongly suggests that this family has hereditary hematuria, nephropathy and deafness. We shall withhold judgment until more members of the family have been studied. If the family does have hereditary hematuria, nephropathy and deafness, the suggestion that this disease occurs only in Anglo-Saxons is invalid.

The pathologic renal factors associated with hereditary hematuria, nephropathy and deafness have not been studied adequately. None of the members affected in the families reported by Guthrie[4] or by us were studied at autopsy. Reyersbach and Butler[3] mentioned that "post-mortem examinations disclosed shrunken kidneys." A description of microscopical findings was not given. They reported that biopsy of the kidney on a two-year-old boy showed only many fresh red blood cells in the tubules. Because of the lack of precise pathological information we are forced, at present, to call the renal disease a "nephropathy."

The term "nerve deafness" is used in this paper to indicate deafness due to involvement of the auditory

nerve or the organ of Corti. The bilateral nerve deafness in patients with this disease has varied from losses of 30 to 50 decibels in our patient to the severe deafness of one of Alport's[7] patients, whom he described as "stone deaf." Clinical observations suggest that the deafness is progressive. At present there are no audiometric data to substantiate this observation. The pathologic factor causing the deafness is unknown. However, Sohar's[10] observation of positive recruitment suggests involvement of the organ of Corti.

The data concerning the families reported by Alport,[7] Reyersbach and Butler[3] and ourselves reveal that 24 of the 30 males with familial renal disease were deaf. The 6 males with renal disease whose cases were reported by Sohar[10] were also deaf. In the family studied by Alport[7] 3 males with familial renal disease were said not to be deaf although they had not been studied for deafness. It is possible that they were deaf but that deafness was not recognized. Reyersbach and Butler[3] reported that 12 of 15 males with familial renal disease whom they had studied were deaf. The 3 who were not deaf were three, three and six years of age; deafness may develop as they grow older. This occurred in the 2 uncles of our patient who became deaf in their teens. The 8 males with familial renal disease in our patient's family were deaf. All the data suggest that the male patients with the syndrome are almost always deaf.

Transmission of the disease in the families reported by Guthrie,[4] Reyersbach and Butler[3] and ourselves has been by the females, both affected and nonaffected. This is also true of the family reported by Sohar.[10] Further study of many kinsmen of our patient is necessary before we can accurately assess inheritance.

Our report is a preliminary one; we have investigated only the descendants of our patient's grandmother. Currently, we are collecting data on 240 other relatives who are descendants of his grandmother's siblings.

## Summary and Conclusions

The condition marked by hereditary hematuria, nephropathy and deafness appears to be a definite genetic entity. The disease is characterized in males by the presence of hematuria, albuminuria, cylindruria, nerve deafness usually, and progressive renal disease; death occurs at an early age. The disease is characterized in females by the presence of hematuria, albuminuria, cylindruria and occasionally nerve deafness; the course of the disease is relatively benign except during pregnancy, when hypertension, edema and other signs of toxemia may occur. Hematuria may be intermittent. Congenital abnormalities of the eye are occasionally associated.

Our patient and 11 other members of his family have apparently had this disease.

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# MEDICAL PROGRESS

## SYPHILIS AND ITS MANAGEMENT

### A Present-Day Problem

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THE venereal diseases are on the rise again. During the last six months of 1954, forty-three states reported an increase in early syphilis or gonorrhea or both.[1] That syphilis is still a nation-wide problem is evident from the United States Public Health Service estimate that as of December 31, 1955, there were approximately 2,000,000 people in the United States with syphilis requiring treatment. During 1955 approximately 86,800 new cases of syphilis occurred among the civilian population.[2]

The foregoing means that a reservoir of infectious syphilis exists in most communities. Because of the limitations of present control methods, this reservoir cannot dry up. Whether it increases or decreases depends on two factors[3,4]: early diagnosis and treatment; and the existence and efficiency of public-health venereal-disease control methods.

There is another group of people with noninfectious syphilis. These persons, although posing no danger to the public health, may suffer serious effects of late syphilis. Thomas[5] states that serious organic disease develops in about 25 per cent of patients with untreated latent syphilis. According to Jordon and Dolce[6] late complications occur in between 20 and 25 per cent of poorly treated latent cases. The symptomatic late cases present an immediate problem of diagnosis, treatment and often rehabilitation.

It is apparent from the foregoing that syphilis will be a serious medical problem for many years. One of the most important phases of its control is the management of positive blood tests. It is our purpose to describe a systematic and practical approach to the management of a patient discovered to have a positive standard serologic test for syphilis.

Four questions immediately present themselves when one is confronted with such a patient:

Does the patient have syphilis?
If so, in what stage is it?
Is it acquired or congenital?
If the patient does not have syphilis, what is the reason for the positive test?

To answer these questions satisfactorily, a complete diagnostic workup is required. Early and late symptomatic syphilis, with objective signs and symptoms, presents definite diagnostic pictures. The latent stage, on the other hand, is the most difficult one to establish because the diagnosis is essentially an exclusion one. In the light of these facts, the various stages of syphilis and the problems unique to each stage require discussion.

#### PRIMARY SYPHILIS

Primary and secondary syphilis should present no serious difficulty in diagnosis provided the physician remembers a few essential facts. The old dictum that any genital lesion should be suspected of being syphilis until proved otherwise still holds good. An equally valid rule of thumb is to suspect primary syphilis if there is an indolent painless lesion that fails to heal in two weeks, irrespective of the part of the body involved. Sad to say, many of the extragenital chancres are missed. The most likely sites of these chancres are the lips, tongue, tonsils, eyelids, face, breasts, anus and fingers.[7,8]

The diagnosis of primary syphilis depends on the alertness of the physician, and it is established by the finding of *Treponema pallidum* on dark-field examination. The blood test may or may not be positive. It is important to distinguish this spirochete from other spiral organisms that may be found on the genitals or in the mouth. On the genitals one must distinguish *T. pallidum* from *T. genitalis, T. calligyrum, Borrelia refringens* and *B. phagedenis.* In the mouth the spirochete of syphilis must be differentiated from *T. microdentium, T. macrodentium* and *T. mucosum.*

Repeated dark-field examinations are necessary to establish the diagnosis, and it is our practice to perform them daily for at least three days on all genital lesions and all suspected extragenital chancres. If the results are still negative, the patient should be tested serologically for at least three months from the last known exposure. Very often when dark-field examinations of genital lesions have been repeatedly negative, aspiration of the enlarged lymph node yields

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positive results. In case of difficulty in identifying organisms, particularly those of extragenital lesions, and especially if the patient is in the seronegative phase, consultation with a syphilologist is indicated. If an expert opinion is not available, the physician should defer diagnosis and treatment until the blood test becomes positive.

When the chancre first appears only 25 per cent of patients have a positive serologic test; at the beginning of the second week approximately 50 per cent become seropositive; this increases to 75 per cent at the beginning of the third week; and by the fourth week all patients who have syphilis will have positive reactions. At this time, also, most patients will be exhibiting signs and symptoms of secondary syphilis.

### Secondary Syphilis

The secondary stage appears within six months, usually six to eight weeks after an infective exposure. An influenzalike syndrome, a generalized eruption and lymphadenopathy spell out the clinical picture. The blood test is always positive. The eruption may last a few weeks to as long as twelve months. This is followed by a period of latency, which, in at least 25 per cent of cases, is interrupted by signs and symptoms of clinical secondary relapse. Of these patients, again, a little more than a fifth experience one to three additional relapses.[9] However, syphilis in this stage often masks its manifestations. The influenza-like syndrome may not be complete, and the rash may assume peculiar configurations, particularly in late secondary syphilis. A sore throat may continue without interruption for as long as a year, so that any sore throat persisting for two weeks or more calls for a blood test. The eruption may change in configuration and distribution with age. Any rash, irrespective of its apparent nonsyphilitic nature, demands a blood test on the first visit.

### Late Syphilis

Late (tertiary) syphilis may occur in the following forms, either singly or in combination: mucocutaneous, osseous, visceral, cardiovascular and neural. For example, one often finds late mucocutaneous and osseous syphilis occurring together, as in perforation of the hard palate. These two types in turn may coexist with cardiovascular or asymptomatic neurosyphilis. With late mucocutaneous lesions, one seldom sees concomitant general paresis, tabes or chronic meningovascular syphilis. However, patients with cardiovascular syphilis, particularly with aortic insufficiency, more often than not have concurrent neurosyphilis. Thus, since syphilis may appear anywhere in the body, it is obvious that a blood test should be a routine part of every medical examination.

There are, however, limitations of the blood test in late (tertiary) syphilis. About 10 per cent of patients with late benign syphilis (mucocutaneous, osseous and visceral), 20 per cent of those with cardiovascular syphilis and 33 per cent of those with clinical tabes have a negative reaction.

### Latent Syphilis

Latent (asymptomatic) syphilis is the heart of this discussion. It is defined by the Massachusetts Department of Public Health as "a symptomless infection characterized by repeated positive standard blood tests for syphilis with negative spinal fluid serologic findings." Latent syphilis is defined as early if the patient has had a primary or secondary lesion within four years or is less than thirty years of age. It is termed late if there was a primary or secondary lesion four or more years previously or the patient is thirty years of age or older.[10]

Thus, there are three essentials for the diagnosis of latent syphilis:

The patient is asymptomatic (there are no lesions of primary, secondary or late syphilis and no disease or condition causing a biologic false-positive reaction).

The patient has repeated positive blood tests.

The spinal-fluid Hinton or Wassermann test is negative.

### Nature of Blood Test

The purpose of the blood test for syphilis is to detect a particular antibody called reagin (because it reacts). This antibody appears in the gamma-globulin fraction of the blood and, to a lesser extent, in the beta-globulin fraction.[11] It appears early in the course of primary syphilis, as described above, and increases in amount as the patient enters the secondary stage. Unfortunately, reagin also appears in detectable amounts with standard tests for syphilis in nonsyphilitic diseases, the biologic false-positive reactions, which are discussed below. Thus, reagin of itself is not diagnostic of syphilis.

The antigens used for the estimation of reagin are lipids extracted with alcohol from mammalian tissues or even fish or plants. Today, most tests (except the Kahn test) employ a purified material from beef heart called cardiolipin (Pangborn[12]), which contains 4 per cent phosphorus but no nitrogen and is alcohol soluble and acetone insoluble. To it are added purified lecithin and cholesterol. Both cardiolipin and lecithin as now used meet the chemical and serologic assay standards of the World Health Organization.[13]

There are two types of standard blood tests for syphilis, the complement-fixation and flocculation tests:

The complement-fixation test is based on the fact that reagin-containing sera fix complement in the presence of cardiolipin antigen. An example is

the familiar Kolmer–Wassermann test. Historically, this is the older of the two types of tests and was described by Wassermann, Neisser and Bruck in 1906. It is based on the phenomenon of hemolysis described by Bordet in 1898 and of complement fixation described by Bordet and Gengou in 1901.

The flocculation tests (precipitation, agglutination) are based on the fact that particles of lipid antigen remain dispersed in normal serum but combine with reagin to form visible aggregates, particularly when shaken or centrifuged. The tests most commonly used in the United States are the Hinton, Kahn, Kline, Mazzini, Rein–Bossak, and V.D.R.L. tests.

Historically, Michaelis, in 1907, a year after the observations of Wassermann and his group, noticed that a precipitate sometimes formed when aqueous liver extract was added to syphilitic serum in the course of the test. In 1910, Jacobstahl, Bruck and Hidika observed that when an alcoholic extract of either syphilitic liver or guinea-pig heart was diluted with salt solution and added to syphilitic serum, aggregates of microscopically visible lipoid particles are formed. This aggregation is the basis of the various flocculation tests for syphilis, but it was not until 1922 that any test of this kind was made sufficiently delicate to be regarded as a safe substitute for the Wassermann test.

The antigen used in both the complement-fixation and the flocculation tests is a lipoid extract of dried beef heart. The fact that positive tests are usually specific for syphilis suggests that lipoid extracts of animal tissues, so far as laboratory procedures are concerned, have much the same antigenic activity as treponemes.

## Lumbar Puncture

The examination of the spinal fluid is the third element in establishing the diagnosis of latent syphilis. Ordinarily, a lumbar puncture is an outpatient or office procedure, after which the patient returns home or to work. Postlumbar-puncture headache is no more frequent — in fact, it seems to be less — with this ambulatory method than it was when the patient was kept in a hospital for six to eight hours and placed in a bed in reverse Fowler's position.[14-16]

A needle of 20 to 22 gauge may be used for a lumbar puncture, preferably the latter. The needle may be inserted while the patient is sitting up on the edge of a table, sitting on a chair with his arms draped over the back or lying on a table on his side with his knees drawn up. From 5 to 8 ml. of spinal fluid should be withdrawn. The spinal fluid is examined for cell count, protein estimation, total protein, Wassermann or Hinton reaction and colloidal-gold curve. The first two procedures may be done at the bedside, and the last three at the laboratory.

### Cell Count

The cell count is the most important single test to be performed. It should be done an hour or so after withdrawal of the spinal fluid. The upper limit of normal is 9 lymphocytes per cubic millimeter.

### Protein Estimation

The second office or clinic examination of the spinal fluid is the total-protein estimation, usually the Pandy test. This test is not and should not be a substitute for the total-protein determination. It is fast and simple. To 1 ml. of Pandy's solution several drops of spinal fluid are added. A bluish-white cloud indicates an abnormal amount of globulin.

### Total Protein

The spinal-fluid protein determination is second in importance to the cell count in estimating the degree of active inflammation of the nervous system. Together with the cell count it constitutes a reliable index of the response to treatment.[17]

### Spinal-Fluid Test

The spinal fluid Wassermann or Hinton test is essential. This, if positive, is indicative of syphilis. False-positive reactions are rare, and when they occur are found in well known neurologic conditions.

### Colloidal-Gold Test

This test is useful but not indispensable. It is nonspecific and by itself cannot prove or disprove the diagnosis of neurosyphilis. However, taken together with the other spinal-fluid tests — cell count, total protein and serologic reaction — the colloidal-gold test confirms the presence of neurosyphilitic damage. It may help also to corroborate and at times may indicate the form of neurosyphilis. In addition, the test may be used to follow response to treatment.

Ordinarily four types of reports are given by a laboratory:

*Paretic or first-zone curve.* The numbers read high to the left, such as 5555542100. Of the four curves, this is the most informative. The paretic curves are seen most frequently in general paresis but may be found in any form of neurosyphilis. They may also be encountered in such nonsyphilitic diseases as multiple sclerosis (50 to 60 per cent), epidemic encephalitis and poliomyelitis.

*Syphilitic, tabetic or mid-zone curve.* The numbers read high in the middle and low at the ends, such as 0123100000 or 0123321000. The mid-zone curves are seen oftenest in forms of neurosyphilis other than paresis, but occasionally they are present even in general paresis. More frequently, they are found in tabes, chronic meningovascular syphilis and such nonsyphilitic diseases as multiple sclerosis (10 to 30 per cent).

*Meningeal curve.* The numbers read low at the left and high on the right, such as 0000123100 or 0012345555. This curve may be seen in bacterial and viral meningitis, encephalitis, brain tumor and multiple sclerosis.

*Normal or flat curve.* This may read as 00000-00000 or 0001100000.

Essentially, abnormal colloidal-gold curves indicate that there is an abnormality in the spinal-fluid protein that has disturbed the albumin-globulin ratio. It is therefore used to supplement the cell count and total-protein determinations, but it should not be substituted for these more sensitive and informative tests.

## Management of Positive Serologic Tests

A positive serologic report in a patient suspected of having syphilis is a welcome confirmation of a clinical diagnosis. The hitherto unsuspected case, the patient in whom a positive serologic test for syphilis was an incidental and accidental finding, is another matter. Four logical and well established procedures are necessary for intelligent management: history; physical examination; laboratory procedures; and epidemiology.

### History

The main objectives of history taking are to ascertain whether the patient has had syphilis before; to learn what treatment, if any, was given; to elicit information about previous blood tests; to find out whether there is a family history of syphilis; and to ascertain whether the patient has had any other venereal disease, such as gonorrhea.

*History of syphilis.* The patient is asked, by the name of the disease and by clinical signs and symptoms, whether he ever had syphilis. What language is to be used by the examiner depends on the individual patient.

The following questions should be included: Have indolent sores appeared on the genitals or other parts of the body, persisting for two weeks or more? Has there been a sore throat that lasted two weeks or more? Has there ever been a generalized eruption on the face, body, palms or soles of the feet that did not itch and was not painful? Was there alopecia?

*Former treatment.* The patient is asked if any hip or arm injections have been given over a period and if a course of penicillin was ever given. It should also be ascertained if, as a child, he was taken to a hospital or doctor's office regularly over a period.

*Serologic history.* Questions on this point are as follows: Has the patient ever had a blood test? When, where and for what? What were the results? Is the patient married or single? If married, when? The premarital-blood-test law was passed in Massachusetts in 1941. If the patient was married since that year, the name of the physician who made the premarital test and the result should be obtained, as well as the result of the premarital blood test of the spouse; if the spouse is dead, one should find out where and when death occurred and its cause, if known.

The history of pregnancy should include questions whether there was a miscarriage or stillbirth, where prenatal care was given, the date and place of delivery and the result of the prenatal blood test (the prenatal-blood-test law was passed in 1939).

The patient should be asked if there has been any hospitalization. If so, a record can be examined for results of the blood test. Such a test is part of the admission workup in any well run hospital.

If the patient was a blood donor, it should be ascertained when and where the blood was given and if the blood was ever rejected.

The patient should be asked if he served in World War I or II or the Korean War and if he was examined by Selective Service. Did he have any repeated blood tests?

Finally, the serologic history should reveal if any other medical examination, by a private physician, insurance company, industrial physician and so forth, was followed by questions regarding the blood.

*Family history.* Is there a history of syphilis among parents or siblings, by name and by signs and symptoms?

*Other venereal disease.* Did the patient have any other venereal disease, such as gonorrhea?

*(To be concluded)*

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# MEDICAL INTELLIGENCE

## CONGENITAL ABSENCE OF THE SPLEEN IN AN ADULT*

### Report of a Case Associated with Recurrent Waterhouse–Friderichsen Syndrome

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PHILADELPHIA

CONGENITAL absence of the spleen is a rare and interesting anomaly that has been reported in both infants and adults. The infantile cases are almost invariably associated with serious congenital malformations of the cardiovascular, gastrointestinal and pulmonary systems that are incompatible with long life. These include atrioventricularis communis, pulmonary stenosis or atresia, anomalies of the aorta and great vessels, complete or partial situs inversus, anomalies of the mesentery and accessory lobes of the lungs. In the adult, splenic agenesis is usually an isolated and unexpected finding.

In a comprehensive review of the literature up to 1952, Polhemus and Schafer[1] found 26 verified cases of congenital absence of the spleen. Of these, 16 occurred in infants, and 10 in adults. Since this report, 8 additional cases of splenic agenesis, all occurring in infants in association with major congenital anomalies, have been reported.[2-7] Of the 10 adult cases, only 2 have been reported since 1918,[8,9] and only 1 has been described in the American literature.[8]

#### CASE REPORT

F.D., a 36-year-old man, was admitted to another hospital on January 27, 1955, with the signs and symptoms of an acute meningoencephalitis. A Type 22 pneumococcus was cultured from the spinal fluid and blood. The patient had an extremely stormy course complicated by the development of the Waterhouse–Friderichsen syndrome, but eventually responded to vigorous therapy, which included antibiotics, gamma globulin, cortisone and aqueous adrenal extract. No primary focus for the infection was found, although there was a history of pneumonia on 2 occasions during the preceding year. Agammaglobulinemia was suspected because of a past history of frequent attacks of "measles" and respiratory infections. Serum electrophoretic patterns were not obtained, but the total serum protein and albumin-globulin ratio were normal.

The patient was transferred to the Philadelphia Veterans Administration Hospital on March 24. Physical examination revealed a poorly nourished, lethargic man. There was marked mental deterioration. He seemed to comprehend vocal commands but was unable to speak more than a few words. He was incontinent of urine and feces. Generalized motor weakness, especially of the lower extremities, was present. There was a large presacral decubitus ulcer.

Results of laboratory studies were within normal limits except for the presence of persistent pyuria due to a urinary-tract infection with *Proteus vulgaris*.

Therapeutic emphasis was given to mental and physical rehabilitation and treatment of the decubitus ulcer and urinary-tract infection. There was a slow but steady response to therapy. The patient became ambulatory and showed improvement in his speech and reading ability although he did not regain his previous intellectual status.

On June 24 he was sent home on a 10-day convalescent leave to determine whether further rehabilitation would be better accomplished in his home atmosphere. At that time he had been afebrile and apparently free of infection for 2 months.

On June 30, chilly sensations and a temperature of 100°F. developed. At the time of readmission to the hospital 5 hours later, the temperature had risen to 106°F., and he was in deep coma. The blood pressure was 60/40; the pulse was 160, and the respirations 36. Other positive physical findings included nuchal rigidity, pharyngeal injection and rales at the base of the left lung. The remainder of the physical and neurologic examination was not remarkable.

Examination of the blood showed a hemoglobin of 13.5 gm. per 100 ml., a hematocrit of 44 per cent and a white-cell count of 6800, with 82 per cent neutrophils. Urinalysis revealed a slightly positive test for albumin and 1 or 2 white blood cells per high-power field in the sediment. On lumbar puncture clear colorless spinal fluid was obtained under an initial pressure equivalent to 80 mm. of water. Examination of the fluid revealed 8 lymphocytes per cubic millimeter, with a protein of 85 mg.; sugar of 71 mg. and chlorides of 696 mg. per 100 ml. Direct smears of the cerebrospinal fluid were negative for organisms, and cultures revealed no growth. On the following day examination of the blood disclosed a white-cell count of 35,100, with 98 per cent neutrophils. The serum sodium was 129 milliequiv., the serum potassium 3.8 milliequiv., and the serum chloride 111 milliequiv. per liter. A blood culture was sterile. The serum protein and electrophoretic pattern were normal (the patient had received 500 ml. of plasma before these determinations).

He was treated with oxygen, plasma, intravenous infusions of fluids and electrolytes, penicillin, oxytetracycline, sulfadiazine and streptomycin. Hydrocortisone, nor-epinephrine, whole adrenocortical extract and desoxycorticosterone were administered intravenously in a vain attempt to maintain adrenal function. There was no apparent response to therapy. Generalized ecchymoses developed, and the patient lapsed into profound shock and died 24 hours after his return to the hospital.

Post-mortem examination§ revealed ecchymoses involving the skin and most of the viscera. A right-upper-lobe pneumonia was present. Both adrenal glands were enlarged to 1½ times their normal size, and large confluent areas of hemorrhage were apparent on the cortical surfaces. Cut section showed that the normal adrenal architecture had been altered by hemorrhage. A purulent cystitis was present. The pia arachnoid was thickened and fibrosed over both cerebral hemispheres and at the base of the brain. Three foci of hemorrhagic necrosis were observed on the superior portion of the cerebral hemispheres. A careful search failed to reveal the presence of a spleen or accessory spleens. A small branch of the celiac axis coursed over the superior aspect of the pancreas, supplying the pancreas and the surrounding tissues. There was generalized lymph-node enlargement.

Microscopical examination confirmed the diagnosis of pneumonia and bilateral adrenocortical hemorrhages. There was evidence of old and probably acute meningitis. A thorough microscopical search of the fatty areolar tissue in the left upper quadrant yielded no evidence of splenic tissue.

The significant pathological diagnoses were acute and healed meningitis; bilateral adrenocortical hemorrhage (Waterhouse–Friderichsen syndrome); pneumonia, right upper lobe; purulent cystitis; and congenital absence of the spleen.

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## Discussion

Like that of most anomalies, the etiology of splenic agenesis is obscure. The spleen appears in the embryo at about the fifth week as a localized thickening of the mesoderm on the left side of the dorsal mesogastrium. The major changes concerned with elaboration of cardiac septum and valves, leading to formation of a four-chambered heart, rotation of the gut and formation of all the bronchial buds, have not been completed at this age.

There is no record of abnormalities of the maternal course during pregnancy in any of the reported cases of congenital absence of the spleen. The only sibling of 1 of the infants described by Polhemus and Schafer[1] died with cyanotic congenital heart disease at the age of eleven months. Autopsy of this sibling revealed atrioventricularis communis, multiple accessory spleens and partial transposition of the abdominal viscera. Though this suggests some basic defect in the germ plasm, no other similar familial occurrence is on record.

The relation of the frequent infections and recurrent Waterhouse–Friderichsen syndrome of this patient to the absence of his spleen is conjectural. The spleen is usually assigned a part in the defense mechanism of the body, probably through antibody formation. There is good evidence of this in some animals.[10] In rodents, for example, removal of the spleen is said to interfere with the development of an immune response to an extent that appears to depend largely on the species of animal, the route by which the antigen is administered and the number and size of the doses of antigen given.[11] Lead shielding of the spleen of rabbits or rats during total body irradiation prevents the reduction of circulating antibody concentration that usually occurs under this circumstance.[12]

Rowley[13] has demonstrated that splenectomized human beings fail to respond with a significant rise in antibody titer when an antigen is given intravenously. Clinically, however, there is no evidence that such patients are more susceptible to infections than normal persons.

It is interesting that of the 10 reported adult cases of congenital absence of the spleen in adults, death has resulted from some disease involving the lymphatic system in 7—tuberculosis,[14-16] typhoid fever,[17] malaria[18] and lymphosarcoma.[8,19] In the other 3 cases splenic agenesis was an incidental finding.[20-22] In the case presented above, there was no other apparent reticuloendothelial abnormality other than generalized lymph-node enlargement due to reactive hyperplasia.

## Summary

A case of congenital absence of the spleen in an adult is presented. Ten previous cases have been reported in the literature.

The possible relation of splenic agenesis to this patient's history of frequent infections and recurrent Waterhouse–Friderichsen syndrome is discussed.

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# A PRACTICAL METHOD FOR THE ASEPTIC PREPARATION OF HUMAN PLATELET CONCENTRATES WITHOUT LOSS OF OTHER BLOOD ELEMENTS*

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BOSTON

As a further modification[1] of the method described by Gardner, Howell and Hirsch,[2] a closed plastic system (Fig. 1) has been designed for the primary purpose of concentrating human platelets. At the same time the separation of other blood elements and the aseptic removal of aliquots of whole blood or blood components are facilitated. This system eliminates the risk of contamination and mismatching of red cells and plasma.

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The donor's vein is entered by means of a needle coated with a hemo-repellent agent.* After the steel ball is released, the blood enters the first bag, where it is mixed with an appropriate anticoagulant solution, and is prevented from leaving this bag by a clamp and a diaphragm. When 500 to 550 ml. of blood has been collected, the whole assembly is placed in a centrifuge cup with the connecting tubing pointing upward (second insert, Fig. 1). The red cells are sedimented, leaving a platelet-rich supernatant plasma (1200 r.p.m. for twenty minutes — International Centrifuge, Model PR 2).

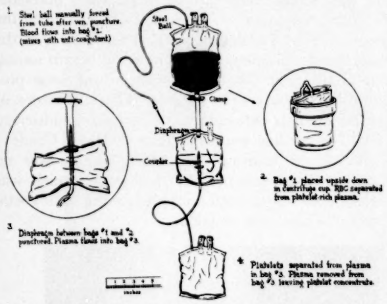
1. Steel ball unusually forced from tube after vein puncture. Blood flows into bag #1. (mixes with anti-coagulant)
Steel Ball
Clamp
Diaphragm
Coupler
2. Bag #1 placed upside down in centrifuge cup. RBC separated from platelet rich plasma.
3. Diaphragm between bags #1 and #2 punctured. Plasma flows into bag #2.
4. Platelets separated from plasma in bag #2. Plasma removed from bag #2 leaving platelet concentrate.
inches

FIGURE 1. *Plastic-Bag Assembly for Separating Blood Components.*

The diaphragm is then punctured by the insertion of the coupler, thus establishing continuity between the first and third bags, and the platelet-rich plasma is expelled into the third bag (Fig. 1, third insert). When the white-cell-rich interphase is reached, the coupler may be removed from the connecting tube, and the buffy coat can be allowed to enter the second bag, from which it may be removed through the tab on this bag.

The assembly is now centrifuged to sediment the platelets, which are packed at the bottom of the third bag (2500 r.p.m. for forty minutes — International Centrifuge, Model PR 2). The platelet-depleted plasma is returned into the second bag if plasma and packed cells are desired as separate entities. Alternately, the plasma may be returned into the first bag to obtain reconstituted whole blood.

The recovery of platelets in the concentrates is between 60 and 70 per cent, with an average of 67 per cent. The rates and duration of centrifugation are currently under investigation to determine optimum conditions for platelet separation.

*Arquad 2-C, available from Armour Laboratories, Incorporated, Chicago, Illinois.

Platelet concentrates and other blood elements obtained by this method have been extensively employed for clinical and investigative use.†[1] The platelet-depleted whole (reconstituted) blood has been used for routine blood transfusions. The plasma prepared by this method has been employed in the treatment of hemophilia, as well as for other clinical purposes. This assembly also facilitates the aseptic removal of aliquots of whole blood (or blood components). The possible effect of the second centrifugation on the red blood cells has not yet been investigated. The centrifugal force employed here, however, is of the order of magnitude used in the routine separation of plasma and packed cells.

The ease of platelet separation by this method permits its incorporation into the routine of blood banking. The closed system ensures asepsis during processing and therefore eliminates loss from contamination. The resultant economy is further reflected in the easy availability of other separated blood constituents as by-products of the separation of any one of the formed blood elements.

It is hoped that this basic unit can be adapted to such processes as plasma fractionation and the low-temperature storage of red cells, white cells and platelets.

## SUMMARY AND CONCLUSIONS

The following procedures can be carried out simultaneously, successively or alternately in the closed system described: preparation of platelet concentrates; preparation of packed red blood cells; separation of the buffy coat; preparation of cell-free plasma; reconstitution of one or more blood elements without risk of mismatching; and removal of aliquots of whole blood or of blood elements.

The closed system eliminates the risks of contamination usually inherent in procedures that require multiple entries into the primary blood container.

We are indebted to Drs. L. K. Diamond and D. Howell, of the Department of Hematology, and to Dr. R. Toch, of the Tumor Therapy Division, Children's Medical Center, for their advice and co-operation in the preparation of this report.

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†Part of this work has been presented in a report entitled "The Transfusion of Platelets and Their Frozen and Lyophilized Derivatives in Patients with Thrombocytopenia," presented at the Second Conference on Platelets, National Research Council, Washington, D.C., November 18, 1955.

# CASE RECORDS
## OF THE
# MASSACHUSETTS GENERAL HOSPITAL

**Weekly Clinicopathological Exercises**

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

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## CASE 42241

### PRESENTATION OF CASE*

A seven-year-old girl was admitted to the hospital because of fatigue.

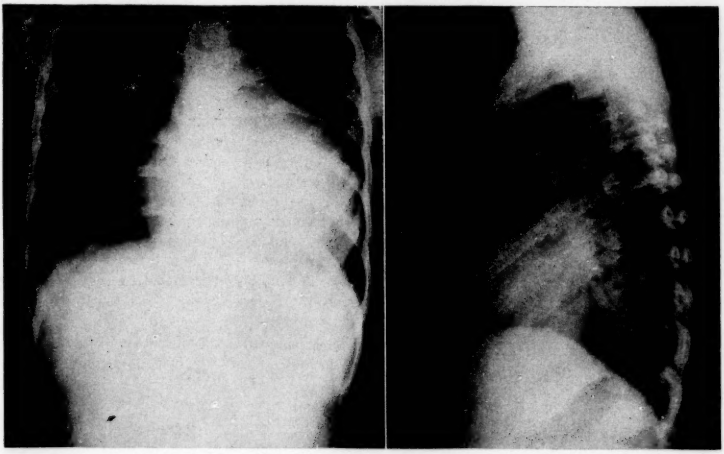

FIGURE 1. *Roentgenograms of the Chest, Showing the Greatly Enlarged Cardiac Shadow.*

Four months previously a sore throat with a temperature of 104°F. that subsided after three days of penicillin therapy developed. Since then at weekly intervals there were temperature elevations to 103°F. associated with chilly feelings. On each occasion there was a good response to antibiotic therapy. One month before admission there was an episode of otitis media with cervical lymphadenopathy. An x-ray film of the chest a week before entry was said to have shown an enlarged heart and normal lungs. During the week before admission pain and swelling in the epigastrium, anorexia, fatigue, moderate dyspnea, pleuritic precordial pain and puffiness of the face were noted.

There was no history of rheumatic fever, chorea or joint pain. There was no known exposure to tuberculosis, scarlet fever or diphtheria.

Physical examination revealed a well developed, slightly pale girl. The tonsils were moderately enlarged and injected, with flecks of white exudate on the right. The veins of the neck were markedly distended two thirds of the way to the jaw when the patient was in a sitting position. Examination of the chest showed dullness, with diminished breath sounds and tactile fremitus, over the right-lung base posteriorly. No rales were audible. The left border of cardiac dullness extended 8 cm. from the midsternal line. The cardiac sounds were muffled. A Grade 1 aortic systolic murmur was heard. There was no friction rub or gallop. The liver edge, which was slightly tender, extended 4 cm. below the right costal margin. There was no edema.

The temperature was 102.2°F., the pulse 160 and regular, and the respirations 28. The blood pressure was 100 to 120 systolic, 70 diastolic, with 20 mm. of paradoxical effect on normal respiration.

The urine was normal. Examination of the blood revealed a hemoglobin of 10.3 gm. per 100 ml. and a white-cell count of 13,500, with 72 per cent neutrophils. The sedimentation rate was 21 mm. per hour. Examination of the bone marrow was negative. Heterophil-antibody agglutination was + at a titer

*Presented at a meeting of the New England Pediatric Society, Boston, March 21, 1956.

of 1:16. Widal and brucella agglutination tests were negative. Four blood cultures showed no growth. An "L.E." preparation was negative. A culture of the throat grew out abundant alpha-hemolytic streptococci, moderate *Neisseria catarrhalis*, a few *Staphylococcus albus* and a few nonhemolytic streptococci; it was negative for *Corynebacterium diphtheriae*. X-ray films of the chest showed generalized enlargement of the cardiac shadow (Fig. 1), with virtually

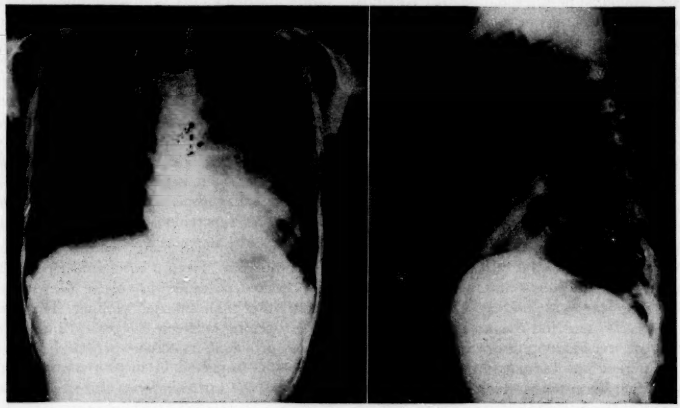

FIGURE 2. *Roentgenograms of the Chest after Aspiration of 400 Ml. of Fluid from the Pericardial Sac. The heart is almost normal in size.*

absent pulsations at fluoroscopy; some free fluid was noted in the right pleural cavity. An intravenous pyelogram was normal. Intradermal tuberculin tests (O.T. 1:1000, 1:100 and 1:10) were negative. An electrocardiogram showed a supraventricular tachycardia at a rate of 155; the PR interval was approximately 0.14 second; there was moderate right-axis deviation; the T waves were flat in Leads 1 and 2, probably inverted in Lead 3, upright in Lead aVL, slightly inverted in Lead aVF, and diphasic in Lead $V_1$; the ST segments were depressed and the T waves were inverted in Leads $V_2$ through $V_4$, with flat T waves in Leads $V_5$ and $V_6$; Lead $V_4$ showed a predominant R wave of low voltage; there was a tendency to low voltage throughout.

A pericardiocentesis on the second hospital day yielded 400 ml. of bloody fluid. A smear stained with Wright's method showed large phagocytic mononuclear cells with pale, vacuolated cytoplasm containing particulate matter. In addition there were occasional clumps of cells five or six times larger than the phagocytic cells with very little cytoplasm and dark-blue-staining nuclei containing nucleoli; many of these cells were multinucleated. A culture was negative; smears were negative for acid-fast bacilli. A cell block was negative for malignant cells, and a cytologic smear was unsatisfactory. After the pericardiocentesis the venous distention subsided, the liver edge was felt 1 cm. below the right costal margin, and the blood pressure was 120 systolic, 60 diastolic, without pulsus paradoxus. X-ray films of the chest showed the heart shadow to be normal in size and shape (Fig. 2). On fluoroscopy pulsations were present but decreased. The temperature ranged between normal and 99.8°F. Streptomycin and isoniazid therapy was started on the eighth hospital day. During the two weeks after the pericardiocentesis x-ray films demonstrated a gradual reaccumulation of pericardial fluid. On the seventeenth hospital day distention of the veins of the neck was again noted, as well as a protodiastolic gallop audible along the upper left sternal border. The venous pressure was equivalent to 210 mm. of saline solution. The white-cell count was normal, and the sedimentation rate 15 and 21 mm. The blood pressure gradually fell to 98 to 90 systolic, 50 to 0 diastolic. On the twenty-first hospital day pericardiocentesis yielded 400 ml. of bloody fluid; with Wright's stain cells identical to those previously seen were noted in the fluid; a cell block and cytologic smear were negative. The patient was transfused with 500 ml. of whole blood. After the pericardiocentesis the venous distention subsided, the pulse was 140, the venous pressure was normal, and the blood pressure was 114 to 112 systolic, 50 diastolic. The liver edge was felt 3 cm. below the right costal margin. X-ray films of the chest showed lessening of the over-all dimension of the cardiac shadow, but there was no return to normal size. An electrocardiogram showed no significant changes. On the day after the pericardiocentesis the temperature rose to 102°F. During the next day

it ranged between 99.2° and 101.4°F. and thereafter between normal and 100.4°F. Two days after the second pericardiocentesis and twelve hours after the blood transfusion jaundice was noted. Examination of the abdomen showed no change in size of the liver. The total serum protein was 7.5 gm., the albumin 5.1 gm., and the globulin 2.4 gm. per 100 ml. The serum bilirubin was 1.4 mg. direct and 4.4 mg. per 100 ml. total. Cephalin flocculation was + in forty-eight hours. The alkaline phosphatase was 4.3 units. Direct and indirect Coombs tests were negative. Examination of the urine showed a negative Harrison spot test. On the next day the serum bilirubin was normal. X-ray films of the chest on the twenty-seventh hospital day showed a further slight increase in the heart shadow.

An operation was performed on the thirty-second hospital day.

### Differential Diagnosis

Dr. Conger Williams*: I saw this patient once during Dr. Friedlich's absence. At this time it was obvious, as it is now, that the differential diagnosis revolved about the conditions that produce cardiac tamponade. The physical findings, including the pulsating neck veins and the really significant paradoxical effect of the blood pressure, pointed to the diagnosis of pericardial tamponade, and this was proved by pericardiocentesis, which yielded bloody fluid and relieved the acute interference with cardiac output. It is no longer believed that blood in the pericardial fluid necessarily means tumor or tuberculosis since many patients with so-called "nonspecific pericarditis" may also have bloody fluid and certainly bloody fluid is rare in a tuberculous pericarditis. The conditions that produce cardiac tamponade may be grouped under broad headings of tumor, infection and hemorrhage. These will be discussed more fully below, but first I should like to dispose of some of the possibilities that can be eliminated easily.

May I see the x-ray films before I discuss the case?

Dr. Joseph Hanelin: The film of the chest taken on the second hospital day before the paracentesis shows a greatly enlarged heart, which is uniformly increased in size (Fig. 1). The lung fields are relatively clear and are characteristic of an uncomplicated pericardial effusion. After the removal of 400 ml. of fluid the heart is virtually normal in size (Fig. 2). Seven days after admission the fluid has partly reaccumulated. The lungs remain clear. The films taken a day or two after the second aspiration of fluid from the heart, during which 400 ml. was again removed, show that the heart is still considerably enlarged.

Dr. Williams: A number of conditions produce pericardial effusion not going on to tamponade. One of these is rheumatic fever. In the numerous cases of rheumatic heart disease with pericardial effusion treated at the House of the Good Samaritan over a fifteen-year period there was only 1 tamponade that required tapping. There was no other evidence for rheumatic fever in the case under discussion. There are a whole series of organisms that produce purulent infection with pericardial tamponade such as the staphylococcus and pneumococcus, but the evidence from the repeated taps is against such an infection. The so-called group diseases—rheumatoid arthritis, lupus erythematosus and sometimes polyarteritis—produce pericardial effusion but rarely tamponade. I never discuss the differential diagnosis of causes of cardiac tamponade without mentioning amebiasis. A medical student at the City Hospital three or four years ago made a correct diagnosis of amebic pericarditis on clinical grounds. Again, I lack evidence for such a diagnosis. A large number of cases are grouped together as nonspecific pericarditis, the etiology of which is obviously unknown. I suspect that it is a diagnostic catchall that may include cases of recurrent tuberculous infection.

An operation was finally performed because fluid reaccumulated. From a mechanical point of view it was deemed necessary to relieve the tamponade by means other than repeated tapping. This can be done by an opening between the pericardium and pleural cavity, provided it seems warranted after the pericardium is inspected. I suspect that another reason for doing the operation was the need for a definite diagnosis. I gather that the streptomycin and isoniazid therapy was begun early in the course of the disease because of the belief that this might have been tuberculous. Many features pointed to tuberculosis: the long febrile illness, the pericardial tamponade that required repeated taps and so on. The absence of obvious pulmonary disease is not against tuberculosis as the etiologic factor. I think in the 3 cases I have seen recently, only 1 patient had any clinical signs or evidence in the x-ray films of tuberculous infection in the lungs. I shall raise the question whether the slow reaccumulation of fluid is somewhat against tuberculosis. Certainly, in the patients whom I have seen with tuberculous tamponade, fluid has reaccumulated much more rapidly than that did. I am sure that varies; moreover, the child was being treated at the time.

Another condition that we always consider in association with tamponade is tumor. In our series of 17 cases, tumor was by far the most frequent etiologic factor. Of course, those patients were adults; this one was a child. Of the tumors I should consider only malignant lymphoma because of recurrent febrile episodes. In spite of the lack of evidence of lymphoma elsewhere in the body it is a possibility that I cannot rule out. The cells found in the pericardial fluid, although not diagnostic, were suggestive of tumor. I know of no other way to make the diagnosis in this case than to look into the pericardial cavity.

*Associate physician, Massachusetts General Hospital.

In any patient who has a long-standing febrile illness, one would think of subacute bacterial endocarditis. The absence of any murmur, of course, is against that. One wonders about the possibility of an infection localizing on a small fistulous congenital vascular channel elsewhere in the body. In view of the fall in diastolic blood pressure, I wonder about involvement of the aortic valve without murmur. I have seen that only once before, and that was in association with syphilis. It would be most unusual for aortic regurgitation on the basis of acute valvular destruction from subacute or acute bacterial endocarditis to be present without a diastolic murmur, particularly in a child. I suspect that the low diastolic pressure had some other cause. Could this child have had a patent ductus arteriosus, which was undetected? We realize now that not every patent ductus produces a machinery murmur, and occasionally these communications are missed. I think this is rather unlikely.

I wonder whether the jaundice represented a hemolytic reaction after the transfusion or whether there was biliary involvement that was undetected. Certainly, the finding would fit with either of those two conditions. I do not believe this was either obstructive jaundice or pancreatitis, in view of liver-function tests and the subsequent course.

I shall narrow the clinical diagnosis to tumor and tuberculosis; I shall favor tumor over tuberculosis and await with interest the results of the surgical procedure.

DR. BENJAMIN CASTLEMAN: By tumor, what do you mean?

DR. WILLIAMS: I think that lymphoma is the best possibility. In one of our previous series we have seen a malignant thymoma that invaded the pericardium. The other possibility is a primary tumor arising in the heart itself. I have never seen this exact picture associated with a primary tumor of the heart. Most of the tumors that we have seen have been on the endocardial surface and produced obstruction to blood flow through the mitral valve or to the pulmonary valve, rather than pericardial effusion.

In the 17 cases of our series of adult patients with cardiac tamponade, 7 were produced by tumor, of which most were ordinary undifferentiated carcinomas; 1 was an oat-cell carcinoma, 1 a mesothelioma, and 1 a malignant thymoma. Of the remaining 10, 3 were tuberculous (2 proved and 1 diagnosed on fairly reasonable evidence), 1 was granulomatous infection, 1 followed myocardial infarction, which does not apply here, and 4 were so-called nonspecific pericarditis.

DR. CASTLEMAN: Would Dr. Shwachman like to comment on the tuberculin test as being against the diagnosis of tuberculous pericarditis?

DR. HARRY SHWACHMAN: I do not believe one can eliminate the diagnosis of tuberculosis because the tuberculin test was negative at this time, for the child was acutely ill.

DR. CASTLEMAN: Do you have any other comment?

DR. SHWACHMAN: I should go along with Dr. Williams's diagnosis.

DR. WILLIAMS: I meant to mention in the differential diagnosis that I did not give any weight to the negative tuberculin test. I thought it was possible that the patient had active tuberculosis and yet had a negative tuberculin test.

DR. CASTLEMAN: Neoplasia in the heart in children is very rare. If I were considering a neoplasm, I should have thought of a metastasis to the pericardium from a neuroblastoma or a Wilms tumor. Dr. Hanelin, can you see any nodularity such as sometimes is seen in the films when tumor involves the epicardium?

DR. HANELIN: Occasionally, nodularity is visible; however, it is not present in this case. We have seen quite a number of patients with pericardial effusion as the result of malignant tumors of one type or another; generally, we visualize only the fluid. It is possible to demonstrate nodules if sufficient pericardial fluid is aspirated and replaced with air.

DR. CASTLEMAN: Dr. Friedlich, you saw this patient; have you a comment?

DR. ALLAN L. FRIEDLICH: Our opinion about the management of this patient was entirely as outlined by Dr. Williams. We were unable to establish the cause of the pericardial effusion. The taps were done in the hope that if this were a benign idiopathic pericarditis, it would quiet down and no further steps would need to be taken. Because of the possibility of tuberculosis we were anxious to have the child on antituberculous therapy in case it became necessary to drain the pericardium. The major difficulty during the first hours that she was in the hospital was to distinguish between congestive heart failure and cardiac tamponade. The chief signs that allowed us to choose tamponade as the most likely explanation were the lack of gallop rhythm in a heart that was tremendously enlarged and the paradoxical pulse, which was of considerable magnitude, about 16 to 20 mm. of mercury. A paradoxical pulse of this degree is usually not demonstrable simply by a palpation of the pulse. One must look for it actively by carefully lowering the pressure in the sphygmomanometer millimeter by millimeter and noting the point at which the pulsations appear in various phases of respiration.

DR. WILLIAMS: One point that was helpful was the clear lung fields noted in the x-ray films.

DR. RALPH A. ROSS: How much help does one receive from examination of the fluid histologically?

DR. WILLIAMS: In the fluids from 2 of our series tumor cells were found. The fluid was not examined for cells in the cases that obviously were not tumor.

DR. CASTLEMAN: The mesothelial cells in any chronic infectious process balloon out and look very much like tumor cells so that the pathologist and cytologist have a great deal of difficulty in distinguishing between a mesothelial cell and a tumor cell.

Is Dr. McGovern here? Would you say a word about that?

DR. JOSEPH J. MCGOVERN: When Dr. Friedlich handed me the tube containing the bloody pericardial fluid, I took it to the laboratory, spun it down and made a smear of the buffy coat. There were large masses of mesothelial cells and sporadic clumps of large multinucleated cells, which I could not identify except to say that they appeared to be tumor cells. I think, from my point of view, that this represented at least a lead in the opposite direction from infection.

DR. CASTLEMAN: Dr. McGovern showed me the slides. I agreed with him that the cells were quite suggestive of neoplasia, but I could not be sure that they were not giant mesothelial cells. With that evidence, since fluid reaccumulated in the heart, this patient was operated on. Dr. Scannell, will you tell us your findings?

### CLINICAL DIAGNOSIS

Pericardial effusion, with cardiac tamponade, probably caused by tumor.

### DR. CONGER WILLIAMS'S DIAGNOSIS

Malignant tumor of heart, probably lymphoma.

### ANATOMICAL DIAGNOSIS

*Fibrosarcoma of heart, right atrium, with pericardial effusion.*
(Cardiac tamponade.)

### PATHOLOGICAL DISCUSSION

DR. J. GORDON SCANNELL: As Dr. Williams has suggested, we explored this patient to establish the diagnosis and to relieve the tamponade by pericardial-pleural drainage or partial pericardiectomy if need be. The pericardial sac was found to be distended by a moderate amount of pericardial fluid. It seemed to be of normal consistence, however, and only slightly thickened by virtue of a lining of fibrinous exudate. The pericardial fluid was frankly bloody. The reason for this was not apparent until I passed an exploring finger over the anterior surface of the heart and encountered a firm, nodular mass about the size of a walnut in the region of the right atrial appendage. To visualize this mass better, we transected the sternum and in this way obtained adequate exposure. The walnut-sized mass seemed to arise in the wall of the atrium, possibly in the atrioventricular groove and therefore in relation to the annulus fibrosus or tricuspid ring. It was intramural, half of it projecting outside the heart and half into the right atrial cavity. The latter is a low-pressure chamber with slack, thin, muscular wall. It was possible to free up the tumor sufficiently to

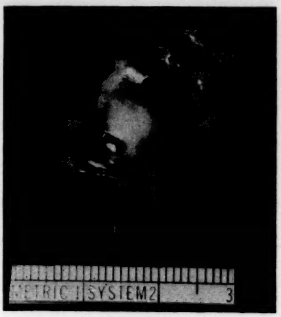


FIGURE 3.

apply Potts clamps so as to excise the tumor with a wedge of atrial wall. This could be done without interruption of the circulation. It was possible to close the resulting defect in the atrial wall with fine

FIGURE 4.

arterial silk, a flap of atrial appendage being used to secure hemostasis. The child tolerated the procedure extremely well.

DR. CASTLEMAN: The mass was about 3 cm. in diameter and appeared to be fairly well circumscribed; a portion of the right atrium was intimately

attached to the tumor (Fig. 3). The cut surface had a homogeneous, almost gelatinous appearance. On microscopical examination the tumor was made up of collagen, in which some areas were acellular but others were quite cellular. Some of the cells were similar to those noted in the pericardial fluid, even including the giant cells, but most of the cells appeared to be mature fibroblasts. Sections through the peripheral portion of the tumor showed it to be invading the muscle fibers of the atrium (Fig. 4).

I think this is a neoplasm rather than an overgrowth of tissue or a so-called hamartoma. The finding of atypical cells and a rare mitosis make me believe it is a fibrosarcoma, perhaps, as Dr. Scannell believes, arising from the ring of the tricuspid valve. The fact that this extended through the atrial wall and produced the pericardial reaction is also in favor of its being a malignant tumor, probably of low-grade malignancy. I have never seen anything like this before. It did not resemble the myxoma, which is the most common tumor of the heart. They are usually pedunculated, are in the left atrium and obstruct the mitral orifice.

DR. WILLIAMS: Do you think that this tumor could have produced the fever, or was that a chance association?

DR. CASTLEMAN: I think the intermittent fever may have been a reaction to the fluid produced by the tumor.

The patient was discharged on the fourteenth postoperative day.

## CASE 42242

### PRESENTATION OF CASE

A forty-seven-year-old man entered the hospital because of swelling of the left testis.

During a routine examination two weeks before admission a painless swelling of the left testis and an abdominal mass in the right lower quadrant were noted. For about fifteen years he had noted "pus" in the urine at the end of voiding in association with "prostate trouble." Except for an occasional, transient pain in the right lower quadrant there were no abdominal symptoms.

Forty-three years previously an appendectomy was performed. Because of apparent sequelae two additional operations were done. Three years before entry he was said to have had amebiasis.

Physical examination showed a well nourished man with a well healed incision over McBurney's point. Superior to the external inguinal ring on the right was a fixed, nontender mass measuring 3 cm. by 5 cm. The left side of the scrotum contained a fluctuant mass that transmitted light and measured 3 cm. by 5 cm. The left testis was identified within the mass. The right testis was in the scrotum. Rectal examination revealed a slightly enlarged prostate.

The temperature was 98°F., the pulse 88, and the respirations 20. The blood pressure was 130 systolic, 80 diastolic.

The urine gave a + test for albumin; the sediment contained 2 or 3 white cells and an occasional red cell per high-power field; culture showed no growth. Examination of the blood revealed a hemoglobin of 15.8 gm. per 100 ml. and a white-cell count of 5800. The nonprotein nitrogen was 30 mg., and the fasting blood glucose 98 mg. per 100 ml. A stool specimen gave a negative guaiac test. An intravenous pyelogram demonstrated a somewhat nodular mass overlying the right side of the sacrum and pelvis and extending beyond the mid-line from a point at the upper margin of the sacrum and below the ischial spine. Lying within the mass were a number of tiny, hazy calcifications. No erosion of adjacent bones was noted. Both kidneys excreted contrast material promptly in good concentration. The right ureter was somewhat widened and displaced medially beginning at the upper margin of the sacrum and extending down to the urinary bladder, which was severely deformed (Fig. 1). An upper gastrointestinal series showed the pelvic mass, which measured 14 cm. in greatest diameter, displacing the ileum upward. X-ray films of the chest demonstrated a small, poorly defined, cystic lesion in the third rib in the posterior axillary line. Barium-enema and sigmoidoscopic examinations were negative.

FIGURE 1. *Intravenous Pyelogram.*
*The right ureter (upper arrows) and the right aspect of the bladder are extrinsically deformed and displaced by the pelvic mass. The calcifications to the right of the lower sacrum are not well defined in the photograph (lower arrow).*

Cystoscopic examination showed some displacement of the bladder to the left. The bladder mucosa appeared normal. A catheter was passed up the right ureter without encountering obstruction. Aspi-

ration of the mass in the left side of the scrotum yielded 120 ml. of white, turbid fluid. After removal of the fluid a normal left testis was felt.

On the seventh hospital day an operation was performed.

### Differential Diagnosis

Dr. Benjamin A. Barnes*: Since the x-ray films produced the best lead to the diagnosis in this case, I should like to ask Dr. Wyman a few questions about the films. Do you agree that the x-ray films exclude, as well as one can by these technics, intrinsic lesions of the urinary tract and of the gastrointestinal tract?

Dr. Stanley M. Wyman: Yes; the urinary passages seem normal intrinsically, the right ureter being displaced greatly toward the mid-line, but without involvement by the mass that overlies the sacrum. Similarly, the cecum is displaced upward and laterally but not invaded, and the terminal ileum is not abnormal except for its location.

Dr. Barnes: Is it possible for you to define any lesion in the bony pelvis that may be related to the diffusely calcified mass on the right side?

Dr. Wyman: The bony pelvis and particularly the portions of the sacrum and ilium adjacent to the mass appear intact.

Dr. Barnes: Is there any evidence in the films of the skeleton of a generalized bone disorder such as a diffuse demineralization?

Dr. Wyman: No; the skeleton seems quite well mineralized, and I see nothing to suggest metabolic or widespread bone disease.

Dr. Barnes: In summary, this forty-seven-year-old man entered the hospital because of a swelling of the left testis, which in all probability was a spermatocele unrelated to the large mass in the right lower quadrant that was present with few symptoms for an undetermined length of time. Physical examination, with a normal temperature, pulse and respirations, gave no evidence of an infectious process. The major finding of a large, nontender, fixed mass in the right lower quadrant was confirmed by the subsequent x-ray studies that apparently indicated the mass to be outside both the gastrointestinal and urinary tracts. The x-ray films are also helpful in outlining the size of the mass, which was approximately 14 cm. in greatest diameter. The negative sigmoidoscopy and cystoscopy confirmed the impression of the radiologists that the lesion was extrinsic to the bowel and to the urinary tract.

It seems highly unlikely that this mass could be accounted for by any congenital defect, and it is tempting to connect the mass with the appendectomy performed forty-three years previously when the patient was four years of age. Because of the two additional operations it is conceivable that certain complications arose at that time that might have been the background for this mass disclosed in adult life. However, the prolonged latent period for a foreign body or an infectious process to manifest itself seems to exclude this operation or its complications as a likely explanation for the patient's condition.

A somewhat more inviting lead is seen in the statement that the patient had amebiasis three years before entry. Amebic lesions outside the gastrointestinal tract are more common in the liver, lung and brain than in the retroperitoneal area. Apart from the fact that there was no x-ray evidence of any active disease in the large bowel to suggest amebiasis, the mass, if it had been an amebic granuloma, should have been in close proximity to the large bowel and not so far removed from the colon. We have no mention in the protocol of stool examinations for parasites or ova.

Calcified retroperitoneal masses are often a sign of tuberculous lymph nodes, but in the absence of any history of a tuberculous infection and in the absence of pulmonary disease or residual changes after pulmonary tuberculosis, tuberculous lymphadenopathy seems a remote possibility as a cause for so large a mass.

Masses in this particular area in relation to the iliac vessels should always be reviewed with the thought of an aneurysm of a major artery in mind. The absence of pulsation and the fine, diffuse calcification are not suggestive of an aneurysm, in which, commonly, the calcification is in curved plaques and assumes a configuration consistent with the outline of the walls of the aneurysmal sac.

The displacement of the right ureter in a medial direction is so pronounced that the possibility of a retroperitoneal neoplasm should next be considered. Among retroperitoneal neoplasms, statistically lipomas and liposarcomas are common, and it is pertinent to consider the present mass as such a lesion. However, other soft-tissue tumors are not infrequent in the pelvis. For benign lesions, a leiomyoma may be retroperitoneal in this area. A leiomyoma may be derived from smooth-muscle elements present in blood vesvels, but it is a distinctly unusual tumor to find in the retroperitoneal area. Rhabdomyosarcomas are occasionally reported as presenting in the retroperitoneum, but their common sites are in areas of the body where the mass of striated muscle is located, particularly in the extremities. Leiomyosarcomas are seen in the retroperitoneal areas, but their recognized potentiality to metastasize early and widely weighs against such a malignant growth as the cause of this large tumor. Fibrosarcomas are predominantly located in the skin and subcutaneous and musculotendinous tissue, and they are more often seen in extremities and occasionally in operative scars. Although not a common finding in the retroperitoneum they do occur there occasionally. Sacrococcygeal chordomas have their highest incidence in males of this patient's age group, and they may calcify as well. The absence of definite skeletal erosion, however, is de-

*Clinical assistant in surgery, Massachusetts General Hospital.

cidedly against this diagnosis. Against a lipoma or liposarcoma is the fact that the series of these tumors reported by Stout,[1] by Farbman[2] and by DeWeerd and Dockerty[3] do not mention calcification in this class of retroperitoneal neoplasms. The calcification of the tumor in the case under discussion is a definite and striking characteristic, although the density of the calcification is not marked. In view of this calcification, I am inclined to believe that this patient had one of the ossifying tumors either derived from bone or periosteum of the pelvis or from a soft-tissue sarcoma that had calcified because of metaplastic activity. Wilson[4] has presented a series of deceptive extraskeletal tumors in which calcium has been deposited. Included was an example of calcification in von Recklinghausen's disease, but there was no evidence of multiple neurofibromas in this patient. It is also conceivable that the tumor in the present case represented an osteogenic sarcoma derived from the coccyx on the right, where there may have been some minimal bone involvement.

### Clinical Diagnosis

? Calcified granulomatous process.
? Malignant lymphoma.

### Dr. Benjamin A. Barnes's Diagnosis

Ossifying soft-tissue tumor of right pelvis.
? Osteogenic sarcoma derived from coccyx.
? Fibrosarcoma with metaplastic bone formation.

### Anatomical Diagnosis

*Malignant lymphoma, Hodgkin's type, of retroperitoneal lymph nodes, with calcification.*

### Pathological Discussion

Dr. Edgar B. Taft: This patient had a large tumor, weighing 490 gm., which was removed surgically. It was lobulated and variegated in appearance and microscopically was typical of malignant lymphoma of the Hodgkin type. The calcification was present in the areas of fibrosis and degeneration. I do not know that calcification is common in Hodgkin's disease. I have seen no reference to it, but it certainly was obvious histologically. The tumor had a pleomorphic cellular pattern with many lymphocytes and plasma cells; in addition it contained the Reed–Sternberg cells, which are diagnostic of this lesion.

Dr. Allen G. Brailey: Did the patient feel the mass himself?

Dr. Wyman: We were told, when these films were discussed before operation, that the abdominal mass was an incidental finding in the patient, who went to a physician because of the spermatocele.

Dr. Taft: Certainly, the discussion in the protocol suggests that the patient's complaint was the enlarged left testis, which in turn suggests that the mass found on routine physical examination was incidental.

Dr. Richard V. Wilson: About calcification in Hodgkin's disease, I have seen it, I believe, twice before in enlarged lymph nodes in the chest; in these cases lymph nodes had been treated with x-ray therapy and subsequently had resolved. I have never seen calcification in lymphoma in this location.

Dr. Taft: Calcification may occur in any area of necrotic tissue; there was a great deal of fibrosis and necrosis in the lymphoma so that I suppose it is not surprising that there was calcification. I do not remember seeing it before in an untreated case of lymphoma.

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## ANNIVERSARY MEETING

THE annual meeting of the Council of the Massachusetts Medical Society took place on May 21, at the Hotel Statler in Boston, as a prelude to the three-day convocation of the Society that opened on the following morning. In line with the new tradition established a year ago the meeting convened at 5:00 p.m., recessed for the Cotting Supper, and continued its deliberations into the evening.

No great controversies shook the Council on this occasion, as has sometimes happened in the past; the discussions that centered around some of the committee reports were mainly for the purpose of clarification.

The Committee on Public Relations recommended an appropriation from the Society to aid the Massachusetts Department of Public Health in the publication of a "Handbook for Physicians." The granting of this tangible sponsorship may be taken as evidence of the lively interest of the Society in matters pertaining to the public health.

The distasteful pharmacy law, as reported by the Committee on State Legislation, is still not entirely satisfactory even as amended but was accepted as the best that could be obtained under present circumstances. The report of the Committee on Public Health was accepted, and its recommendations adopted after considerable discussion. This discussion revolved in part about the recommendation that the Council approve the Rheumatic Fever Program formulated by the Rheumatic Fever Services Committee and approved by the Executive Committee of the Massachusetts Heart Association and the Worcester and Barnstable districts of the Massachusetts Medical Society; assurance was given that the principles of professional relations were in no way jeopardized. The recommendation that the Society sponsor legislation making it compulsory that every ambulance should carry at least one attendant who holds an active certificate that he has taken the Senior Red Cross first-aid course was modified to include "an equivalent course" and was thus accepted.

The Committee on Welfare Problems reported on the never-ending struggle to obtain adequate compensation for physicians attending welfare cases. It endorsed the continuance of the present composition of the Committee, which now consists of 2 members from each district in addition to the 5-man parent committee. In this relation, when the proposal was later made that the Committee on Blue Cross–Blue Shield Problems be enlarged to include an elected member from each of the 20 districts, strong presentments were made regarding the difficulty of bringing such a committee together. Apparently, much can still be said in favor of Edward Everett Hale's concept of the ideal committee as a group composed of three members of whom one is confined to his bed and one is traveling in Europe.

In presenting the newly elected officers attention was again called to the untimely death of the president-elect, Dr. Harold R. Kurth, and the good fortune of the Society in having Dr. Howard F. Root willing to step into his place. Dr. Root, a member of the Council since 1944, is a former president of the American Diabetes Association, vice-president of the International Diabetes Federation and until recently chairman of the Committee on Diabetes of the Society. Also newly elected were Dr. Patrick J. Sullivan, of Dalton, long a councilor and active committee member, as president-elect; Dr. Leopold F. King, of Lowell, as vice-president; and Dr. Paul D. White, of Belmont, as orator.

Under new business a resolution approving the outstanding services to the Commonwealth of the Massachusetts Poliomyelitis Advisory Committee was unanimously adopted.

At the annual meeting of the Society, called together at 2:30 p.m. on May 22, the Secretary reported on the increase in membership from 7360 at this time in 1955 to the present number of 7493, and the president, in his "State of the Union" message, indicated the progress that medicine has made in a hundred and seventy-five years. The successes that have been made in the war against disease, however, have been partly offset by the loss of life and the injuries sustained in traffic accidents, and President Wesselhoeft consequently proposed that the Council establish a committee on traffic safety. In the tributes paid to those individuals and groups who have been of the greatest service to the Society and to the progress of medical service during the past year, the Woman's Auxiliary came in for its well deserved share.

The usual awards to outstanding fourth-year medical students were presented to Mr. Chase N. Peterson, of Harvard Medical School, Mr. Michael Schiff, of Boston University School of Medicine, and Mr. Lawrence C. Salvesen, of Tufts University School of Medicine. The award for "Outstanding Contributions by a Layman to Medical Progress," the second to be given in a five-year period, was made to Mrs. Frances S. Burns, the distinguished special writer of the *Boston Globe* and dean of New England newspaperwomen, after which badges were presented to 42 fifty-year members of the Society.

The Annual Discourse, *"Docendo Discimus,"* by Dr. Merrill C. Sosman, which concluded the exercises of the afternoon, is presented elsewhere in this issue, and the Shattuck Lecture, "Changing Concepts and Practices in the Approach to Diseases of the Digestive Tract," delivered on the following morning by Dr. Chester M. Jones, will appear in a forthcoming issue of the *Journal*.

The Honorable Leverett A. Saltonstall, senior senator from Massachusetts, was guest speaker at the annual dinner of the Society on May 23.

## SIXTEEN TONS

THE first stage of a vast and exciting experiment in medical care has just been completed in the soft-coal fields of West Virginia, Virginia and Kentucky with the dedication of a chain of ten magnificent hospitals constructed at a cost of over $25,000,000. These hospitals with more than 1000 beds will care for a specific group of some 400,000 people — the miners and their families who work and live in the mountains and "hollers" of this area.

This has been done by the representatives of management and labor who jointly administer the millions of dollars that, as royalties on each ton of coal mined, have been contributed to the Welfare and Retirement Fund of the United Mine Workers of America.

The second stage is now beginning. For years, in many of these areas, the camp doctor has had to be content with the most miserable and disreputable of medical facilities. Now, in these new open-staff hospitals, he may work side by side with a full-time staff of specialists recruited from medical schools and medical centers in many parts of the United States. These general practitioners, for the first time, are enjoying the satisfactions of practicing first-rate medicine, and for the first time, too, many patients are experiencing the mysteries and minor indignities that are part of a complete history and physical examination.

For the specialist this is an opportunity to practice and teach and explore in an atmosphere unfettered by tradition and free of the inertia that so often becomes the silent partner of tradition. And in this atmosphere it is hoped that the many other aspects of medical care will be subjected to the continual scrutiny that must be part of any experiment.

Intern and residency programs will be established, and there will be schools for professional and practical nurses. All this, including the cost of hospitalization and specialist care for the beneficiary, will be paid for by the Fund. Some will certainly argue the philosophies on which this program is based, but none can question the vision, imagination and courage of those who have been responsible for its development.

The future of this experiment will be watched closely, for what is learned here must inevitably contribute to the clarification of some of the many problems of medical care that are the concern of everyone.

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## POLIOMYELITIS VACCINATION IN NEW ENGLAND — RÉSUMÉ FOR 1955

THE National Foundation for Infantile Paralysis, Incorporated, through its medical director, has distributed to the state medical societies of New England the record of participation of the New England states in the 1955 vaccine demonstration program conducted with vaccine supplied by the Foundation,

with a grateful and gracious acknowledgment to the physicians of New England for their co-operation.

The record of participation is expressed in tabular form as follows:

| State | 1st Inoculation | 2d Inoculation | Booster Inoculation | Ending Date NFIP Program | Vaccine from NFIP | Percentage of Group from 5 to 9 Yr. Vaccinated |
|---|---|---|---|---|---|---|
| | | | | | *ml.* | |
| Massachusetts | 160,314 | — | 4,928 | — | 346,944 | 39 |
| Maine | 20,281 | 16,895 | 1,247 | 10/26/55 | 45,590 | 24 |
| New Hampshire | 20,192 | 19,623 | 936 | 11/30/55 | 43,470 | 45 |
| Vermont | 17,140 | 14,962 | 860 | 11/22/55 | 34,965 | 48 |
| Connecticut | 99,132 | 87,860 | 19,952 | 12/30/55 | 232,902 | 58 |
| Rhode Island | 33,490 | 22,498 | 1,682 | — | 68,976 | 52 |
| All New England | 350,549 | 161,838 | 29,605 | | 772,847 | 266 |

As is well understood, the practical suspension of activities in Massachusetts after an initial mass inoculation had been undertaken was on the advice of the state advisory committee. This group withheld approval of a continuance of the program until better evidence of the safety of the vaccine was available. This was eventually secured after various changes in the method of manufacture and of testing the vaccine were made.

Accompanying the tabulation of the results of the program is a printed report to physicians by Basil O'Connor, president of the Foundation. The report — entitled "Can Paralytic Polio Be Prevented in 1957?"—presents the problem of prevention as one of logistics and not one of medical science, with the inference that final accomplishment of the end so devoutly to be wished for is now a matter of vaccine production, unrelated to further research.

## THE EBB AND FLOW OF JUSTICE

As of the time of this writing no one knows what will be the fate of the miserable killer, Kenneth Chapin. It is still possible that within the next few weeks, society will have had its revenge for his atrocious deviation from its standards of behavior, and that the law of an eye for an eye and a life for a life will have been satisfied.

Perhaps in a brave new world it is right that there should be a swing away from the temperate and rational administration of justice that permitted Jesse Pomeroy to live out his life at the expense of the state, and places deliberate criminals, conscious of the implications of their crimes, behind bars for varying periods; apparently the Governor's council believes so although there still stands a body of thoughtful if relatively inarticulate citizens who will always question whether justice or vengeance had been dispensed in this case.

The crime has been committed, — a crime without reason, which raises doubts regarding the reasoning ability of the slayer, — and the families of the victims have been made to pay the last full measure of human suffering. The question remains whether a monotheistic society, dedicated to the advancement of human culture and reasonable tolerance, should destroy the defective agent of the crime or protect itself by shutting him away forever.

If simple justice is to be dispensed it should be given without emotion and apart from the confusion engendered by anger, grief or fear; if the quality of mercy is not strained, it should fall on all alike.

Medical Science.—*The Sultan has authorized the formation of a Medical Society at Constantinople, and sanctioned its title as the Imperial Medical Society of Constantinople. The new Institution was started by the English medical men at Scutari.*

Boston M. & S. J. *June 19, 1856*

## MASSACHUSETTS MEDICAL SOCIETY

### DEATHS

Bigelow — Alice H. Bigelow, M.D., of Boston, died on May 10. She was in her eighty-first year.

Dr. Bigelow received her degree from Tufts College Medical School in 1905. She was formerly secretary to the staff of the New England Hospital for Women and Children, a fellow of the American Medical Association and a member of the New England Women's Medical Society.

She is survived by two nephews and a niece.

Cordaro — Benjamin J. Cordaro, M.D., of Holbrook, died on May 6. He was in his forty-first year.

Dr. Cordaro received his degree from the Boston College of Physicians and Surgeons in 1941. He was a former chairman of the Holbrook Red Cross Blood Bank and a member of the staffs of Phaneuf and Goddard hospitals, Brockton.

He is survived by his widow, three sons and a daughter.

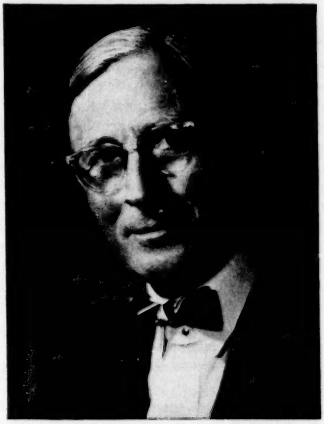
Merritt — Edward Lester Merritt, M.D., of Fall River, died on May 4. He was in his sixty-second year.

Dr. Merritt received his degree from Tufts College Medical School in 1917. He was a former member of the Advisory Council of the Massachusetts Department of Public Health and vice-president of the Massachusetts Society for Crippled Children. He was formerly president and secretary of the Fall River Medical Society and president of Bristol South District Medical Society and chairman of the committees on State and National Legislation of the Massachusetts Medical Society. He was a fellow of the American Medical Association, a censor of Bristol South District Medical Society and a member of the New England Urological Society, American Urological Association, Association of Military Surgeons and American Public Health Association.

He is survived by his widow and three daughters.

Lenscraft Photos

DR. HOWARD F. ROOT, *President*

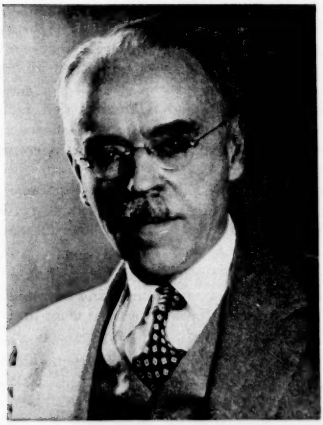


Henzel-Studio

DR. PATRICK J. SULLIVAN, *President-Elect*

Mario

DR. LEO F. KING, *Vice-President*



DR. PAUL D. WHITE, *Orator*

## COMMITTEE ON MATERNAL WELFARE

### Cardiac Decompensation and Multiple Pulmonary Emboli

A thirty-four-year-old gravida II, para I, died four weeks post partum from cardiac decompensation and pulmonary emboli.

The patient had had rheumatic fever in childhood, resulting in mitral stenosis and regurgitation. Her previous pregnancy had been stormy, with an episode of decompensation despite digitalization, bed rest and close prenatal care. Within three months, she was pregnant again and once more received very close prenatal care; dyspnea developed in the seventh month, when she was seen two or three times a week. At thirty-six weeks she was admitted to the hospital with edema and albuminuria. Total weight gain had been limited to 1.8 kg. (4 pounds), and the blood pressure was normal. Treated with bed rest, oxygen, digitalis, mercaptomerin (Thiomerin) and restricted sodium, she began labor spontaneously a week later, delivering, within six and a half hours, a normal infant weighing 2.7 kg. (6 pounds). The second stage of labor was limited to fifteen minutes' duration and was assisted by low forceps with mediolateral episiotomy under low saddle-block anesthesia.

The third stage was immediately followed by uterine atony, which prompted manual exploration and insertion of a uterine pack. This was easily removed on the following day. Post partum, the blood pressure was 120 systolic, 80 diastolic, and the pulse 88, but because of the moderate previous blood loss, 500 ml. of blood was given slowly. Twenty-four hours later, the liver and spleen were greatly enlarged with other evidence of right-sided failure. At this point there were episodes of chest pain and pain in the right leg although Homans's sign remained negative. Heparin and Dicumarol were started as supportive oxygen and similar procedures were continued. Pulmonary edema developed slowly over the next two weeks and was followed by hydrothorax. One month post partum thoracentesis produced 1700 ml. of fluid, but during the next three days the patient's circulatory failure worsened and she died.

Autopsy revealed rheumatic heart disease with mitral stenosis, pulmonary infarcts and edema, thromboses in the myometrial and ovarian veins and other findings typical of cardiac decompensation.

This case was classified as a nonpreventable death. The careful and conscientious prenatal care that was obviously given this patient is impressive. The clinical staff seems to have been faced with an insoluble problem, which gradually became aggravated until death supervened. As in all cases of heart disease the question of advisability of pregnancy arose, and indeed it seems inescapable that the patient would probably still be alive if she had not undertaken the pregnancy. Thus, one might say that the death was preventable in that prior sterilization or early therapeutic abortion in the current pregnancy could have been corrective. However, the immediate cause of death was pulmonary emboli, which occurred in spite of treatment that usually brings such patients through pregnancy alive. It seems doubtful whether valvulotomy would have certainly avoided subsequent pulmonary emboli and even more doubtful whether bilateral-femoral-vein ligation, once emboli became apparent, would have changed the picture in any way except to accelerate the patient's death. With the realization, therefore, that multiple pulmonary emboli are frequently fatal despite the best treatment, the case was considered truly nonpreventable.

John Figgis Jewett, M.D.
*Chairman*

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## WOMAN'S AUXILIARY

Mrs. John C. Angley, of Bryantville, the retiring president of the Woman's Auxiliary, presided at the annual meeting on Tuesday, May 22, 1956, at the Hotel Somerset in Boston. One hundred and sixteen members of the House of Delegates were registered. An increase of 157 members was reported, bringing the membership to 2235 at this time. Forty-two nursing scholarships totaling $7,070 were awarded, and the Auxiliary has sponsored 24 Future Nurses Clubs. Subscriptions to *Today's Health* have increased to such an extent that several districts received national awards.

Mrs. Mason G. Lawson, national president, was the guest of honor. She spoke of the importance of supporting the American Medical Education Fund. She complimented the Auxiliary on its growth and achievement during the past eight years. The following officers for the coming year were installed by Mrs. Lawson: president, Mrs. Roger H. Cheney, Springfield; president-elect, Mrs. Joseph V. Chatigny, Taunton; first vice-president, Mrs. George G. Bailey, Belmont; second vice-president, Mrs. Philip G. Berman, Lowell; corresponding secretary, Mrs. Robert F. Tilley, Brookline; recording secretary, Mrs. Russell F. Sheldon, Boston; and treasurer, Mrs. Erskine S. Pickwick, Fitchburg.

A reception honoring Mrs. Lawson and the past presidents of the Massachusetts Auxiliary was held at the Hotel Statler after the meeting. On Wednesday members enjoyed a trip through the Arnold Arboretum, followed by a luncheon at the Blacksmith Shop in Whitman.

Delegates to the annual meeting in Chicago will be Mrs. John C. Angley, Mrs. A. J. A. Campbell, Mrs. Joseph V. Chatigny, Mrs. Roger H. Cheney, Mrs. John C. Conlin and Mrs. Morton Grant.

## CORRESPONDENCE

### MEANING: AWOL

*To the Editor*: The gobbledygook and abbreviations used in the federal officialese language are w.k. and much commented on. Perhaps the development of a similar but different language in our h. records is not so w.k. This new branch of the language might well be called doctorese. It varies from h. to h. and s. to s. Pretty soon interpreters will have to be obtained by any consultant who sees a patient even in his own h. Here is a prize example from the B.H. of B., M.:

"N.B.: My impression is that this patient's M.S. while enough to produce R.V.H. by Px, has been sorely aggravated by A.S.H.D. which addition has ppt. C.H.F."

If anyone is interested, here is a glossary:

| | |
|---|---|
| N.E.J.M. | *New England Journal of Medicine* |
| B., M. | Boston, Massachusetts (not bowel movement) |
| h. | hospital |
| w.k. | well known |
| s. | service |
| B.H. | blank hospital |
| N.B. | *nota bene* (the only valid abbreviation in this letter) |
| M.S. | mitral stenosis, not morphine sulfate |
| R.V.H. | right ventricular hypertrophy |
| Px. | physical examination, not post-exchange |
| A.S.H.D. | arteriosclerotic heart disease |
| ppt. | precipitated |
| C.H.F. | congestive heart failure. |

V.T.Y.
C.C.L.

B., M.

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### ANNA COLBURN WELLINGTON, M.D.

*To the Editor*: Dr. Wellington died in December, 1955, at the age of seventy-three. After receiving her medical degree from Tufts College Medical School in 1912, she served her internship at the Boston Dispensary Children's Hospital and was associated with the Boston Psychopathic Hospital. During World War I she served with the American Red Cross in France. After that she was associated with the Medfield State Hospital, leaving that post to take charge of a mission hospital in India. In 1925 she became staff physician at Boston State Hospital, transferring to Bridgewater State Hospital in 1926 and then, in 1928, to Grafton State Hospital, where she remained as senior physician until her retirement in 1947.

She performed outstanding service in the development of clinics and classes for children retarded by three years or more in the public schools as required by law. In addition to these she instituted child-guidance clinics and preschool clinics. The results were so successful that many school superintendents, outside the hospital area, requested her services.

Her compulsory retirement at the age of sixty-five was a distinct loss to the school system and the Department of Mental Health.

HARLAN L. PAINE, M.D.

Westborough, Massachusetts

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### REVOCATION OF LICENSE

*To the Editor*: At a meeting of the Board of Registration in Medicine held May 10, 1956, it was voted to revoke the registration of Dr. Douglas H. Cownie, Philadelphia General Hospital, Philadelphia, Pennsylvania.

ROBERT C. COCHRANE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

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## BOOK REVIEW

*Surgery of the Heart.* By Charles P. Bailey, M.D., M.Sc. (Med.), F.C.C.P., F.I.C.S. 8°, cloth, 1062 pp., with 1452 illustrations, 3 color plates, and 45 tables. Philadelphia: Lea and Febiger, 1955. $25.00.

It is fitting that one of the great pioneers in the field of cardiac surgery should be among the first to create a book of outstanding merit on the surgery of the heart. Dr. Bailey is well known for his courage and technical skill. Many of the successes of today in this field are based upon the application of technics and the employment of instruments that are the result of his ingenuity. Thus, many of the procedures described so clearly in this text are naturally his own. Nonetheless, the entire field of cardiac surgery is covered with great thoroughness, and the contributions of others are carefully included.

The book follows a logical arrangement in three parts. The first part includes competent discussions, by collaborators, of the development of cardiac surgery, anesthesia for cardiac operations, cardiac resuscitation and hypothermia. The second deals with the surgery of congenital, and the third with that of acquired heart disease. The numerous illustrations are of uniform excellence. The drawings are diagrammatic and clear. The format of the book is pleasing, and a good index is provided.

It is a great tribute to the abilities of the author that so complete and authoritative a book on a subject that is developing as rapidly as cardiac surgery is today could have been completed at this time. Inevitably, certain technics that have been evolved since the book went to press are not covered, and recent modifications of certain of those described could not have been included. The fact is, however, that this book is as complete and authoritative as it could possibly have been made in the current evolutionary phase of the development of cardiac surgery. It is highly recommended for all who have an interest, whether medical or surgical, in the diseases of the heart.

RICHARD H. SWEET, M.D.

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## BOOKS RECEIVED

**The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.**

*Anatomy for Surgeons.* Vol. 1. *The Head and Neck.* By W. Henry Hollinshead, Ph.D., professor of anatomy, Mayo Foundation, University of Minnesota, and head, Section of Anatomy, Mayo Clinic, Rochester, Minnesota. 4°, cloth, 560 pp., with 326 illustrations. New York: Paul B. Hoeber, Incorporated, 1954. $10.00.

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*Christopher's Textbook of Surgery.* Edited by Loyal Davis, M.D., chairman, Department of Surgery, Northwestern University Medical School. Sixth edition. 4°, cloth, 1484 pp., with 716 illustrations and tables. Philadelphia: W. B. Saunders Company, 1956. $15.50.

# NONCLINICAL NOTES

## MENTAL-HEALTH CENTER

On Sunday, May 13, the Boston Psychopathic Hospital became known as the Massachusetts Mental Health Center (Boston Psychopathic Hospital). This is the new and official name of the hospital as changed by Legislative Acts of 1956.

The change of name does not represent any change in the function of the hospital. Its service to the community and to the Commonwealth will remain unaffected. What has happened, however, is that through the past years there has been a progressive change in the functions of the hospital through the growth of its outpatient department, the Southard Clinic, and the development of a clinic for ex-patients known as Community Clinic. In addition to this, the new wing of the hospital, which was opened in October, 1955, houses both an outpatient and an inpatient treatment center for children. Efforts in preventive work have been stressed. Two floors of the building are devoted to research along psychiatric, psychologic, physiologic and sociologic lines. The basement and fifth floors give expanded facilities for rehabilitation. With these new developments, together with the continuation of the hospital as an intensive treatment, research and educational center, the original name, Boston Psychopathic Hospital, is hardly adequate to cover these expanded functions, and the name Massachusetts Mental Health Center was seen as more clearly communicating the work of the hospital.

# NOTICES

## REFRESHER COURSE FOR GENERAL PRACTITIONERS

A one-month refresher course for general practitioners in clinical medicine will be offered at Beth Israel Hospital, Boston, in August and September. Ward rounds, clinics and conferences will be included in the course. Follow-up studies of patients will be under the supervision of Dr. Nathan Sidel and associates.

Under the provisions of a teaching fund the usual tuition fee will be waived, and a stipend of $250 will be granted, to defray the living costs of the physician during the month of instruction. Further information may be obtained from Tufts Postgraduate Courses, Beth Israel Hospital, Boston 15, Massachusetts.

## WORLD MEDICAL ASSOCIATION AND UNITED STATES COMMITTEE, INC.

The World Medical Association and the United States Committee, Incorporated, announces a change of address to 10 Columbus Circle, New York 19, New York. The telephone number is COlumbus 5-2190.

## INTERNATIONAL COLLEGE OF SURGEONS

The Eastern Sectional Meeting of the International College of Surgeons, United States Section, will be held at the Marshall House and the Emerson House, York Harbor, Maine, July 1-6. Besides the scientific and the educational sessions, many recreational activities have been planned. Further information may be obtained from Dr. M. Leopold Brodny, F.A.C.S., F.I.C.S., 636 Beacon Street, Boston 15, Massachusetts.

## INTERNATIONAL COLLEGE OF SURGEONS

Examinations for qualified fellows of the International College of Surgeons will be held in Chicago, Illinois, July 23 and 24 and October 29 and 30. The oral conferences will be held on August 6 and October 22. Further information may be obtained from the Secretary of the Qualifications Council, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10, Illinois.

## SOCIETY MEETINGS AND CONFERENCES

June 15. New England Pediatric Society. Page 924, issue of May 10.
June 17. American Electroencephalographic Society. Page 924, issue of May 10.
June 18–20. American Neurological Association. Page 875, issue of May 3.
June 18–22. Medical Library Association. Page 1051, issue of May 31.
June 19. South End Medical Club. Page 1104, issue of June 7.
June 19–30. Consultation Clinics for Crippled Children in Massachusetts. Page 1049, issue of May 31.
June 21–23. Society of Nuclear Medicine. Page 1092, issue of December 15.
June 21–24. American Academy of Dental Medicine. Page 994, issue of December 1.
July 1–6. International College of Surgeons. Notice above.
July 9. Fifth Annual Symposium for General Practitioners. Page 1010, issue of May 24.
August 19–23. American College of Chest Physicians. Page 840, issue of November 10.
September 3–5. Congress on Blood Transfusion, Blood Banks and Hematology. Page 297, issue of February 9.
September 10–14. American Dietetic Association. Page 1180, issue of December 29.

### Calendar for the Week Beginning Thursday, June 21

Thursday, June 21
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Dr. John Spellman and staff. Saint Elizabeth's Hospital.
*8:45–9:45 a.m. Cardiac Grand Rounds. Jimmy Fund Building. Children's Medical Center, 35 Binney Street.
*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Medical Grand Rounds. Dr. Sylvester McGinn and staff. Saint Elizabeth's Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*12:00 m. Clinicopathological Conference. Dr. Benjamin Castleman and associates. Pathology Amphitheater, Massachusetts General Hospital.
*12:15–1:15 p.m. Orthopedic Clinic. Amphitheater, Peter Bent Brigham Hospital.
*3:00 p.m. Thoracic Conference. Physiologic Advances in the Management of Patients with Diseases of the Chest. Dr. Maurice S. Segal. Main Amphitheater, Peter Bent Brigham Hospital.

Friday, June 22
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m. Pediatric Grand Rounds. Thorndike Amphitheater, Boston City Hospital.
*12:00 m. Urological Conference. Auditorium, Carney Hospital, Dorchester.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*2:00–3:00 p.m. Pathology Conference. Dr. James Graham. Saint Elizabeth's Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Morton Street, Jamaica Plain.
*4:30 p.m. Neuroradiologic Conference. X-Ray Conference Room, New England Deaconess Hospital.

Saturday, June 23
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:30–11:00 a.m. Surgical House Officers' Conference. Second-Floor Conference Room, Carney Hospital, Dorchester.
*10:30 a.m. Teaching Ward Rounds. Ward South 2, Free Hospital for Women.

*(Concluded on page xxvi)*